AN EVALUATION OF THE CLINICAL PREDICTORS OF THE CARTILAGE INVASION, EXTRA LARYNGEAL SPREAD AND THYROID GLAND INVOLVEMENT IN PATIENTS WITH LARYNGEAL AND HYPOPHARYNGEAL CANCERS (STAGE 3 AND STAGE 4)

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF M.S BRANCH IV OTORHINOLARYNGOLOGY EXAMINATION OF THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY TO BE HELD IN APRIL 2016

DEPARTMENT OF OTORHINOLARYNGOLOGY
CHRISTIAN MEDICAL COLLEGE
VELLORE

DECLARATION

I declare that this dissertation entitled "An evaluation of the clinical predictors of cartilage invasion, extra-laryngeal spread and thyroid gland involvement in patients with laryngeal and hypo pharyngeal cancer (stage 3 and stage 4)''submitted towards fulfilment of the requirements of the Tamil Nadu Dr. M.G.R.Medical University for the MS Branch IV, Otorhinolaryngology examination to be conducted in April 2016, is the bonafide work of Dr. Mohamed Abdul Kathar, postgraduate student in the Department of Otorhinolaryngology, Christian Medical College, Vellore

Dr. Mohamed Abdul Kathar
Postgraduate Student (M S Otorhinolaryngology)
Register Number: 221414354
Department of Otorhinolaryngology
Christian Medical College
Vellore

CERTIFICATE

This is to certify that the dissertation entitled **: '**An evaluation of theaccurate clinical predictors of cartilage invasion, extra-laryngeal spread and thyroid gland involvement in patients with laryngeal and hypo pharyngeal cancer (stage 3 and stage 4)'is a bonafide original work of **Dr M.MOHAMED ABDUL KATHAR,** submitted in partial fulfilment of the rules and regulations for the MS Branch IV, Otorhinolaryngology examination of The Tamil Nadu Dr. M.G.R Medical University to be held in April 2016.

Dr. Alfred Job Daniel

Principal

Christian Medical College

Vellore- 632002

India.

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Dr John Mathew,

Professor and Head,

Department of ENT,

Christian Medical College,

Vellore.

CERTIFICATE

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Otorhinolaryngology examination of The Tamil Nadu Dr. M.G.R Medical University

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Dr Rajiv Charles Michael,

Guide,

Professor& Head,

Department of ENT-1,

Christian Medical College,

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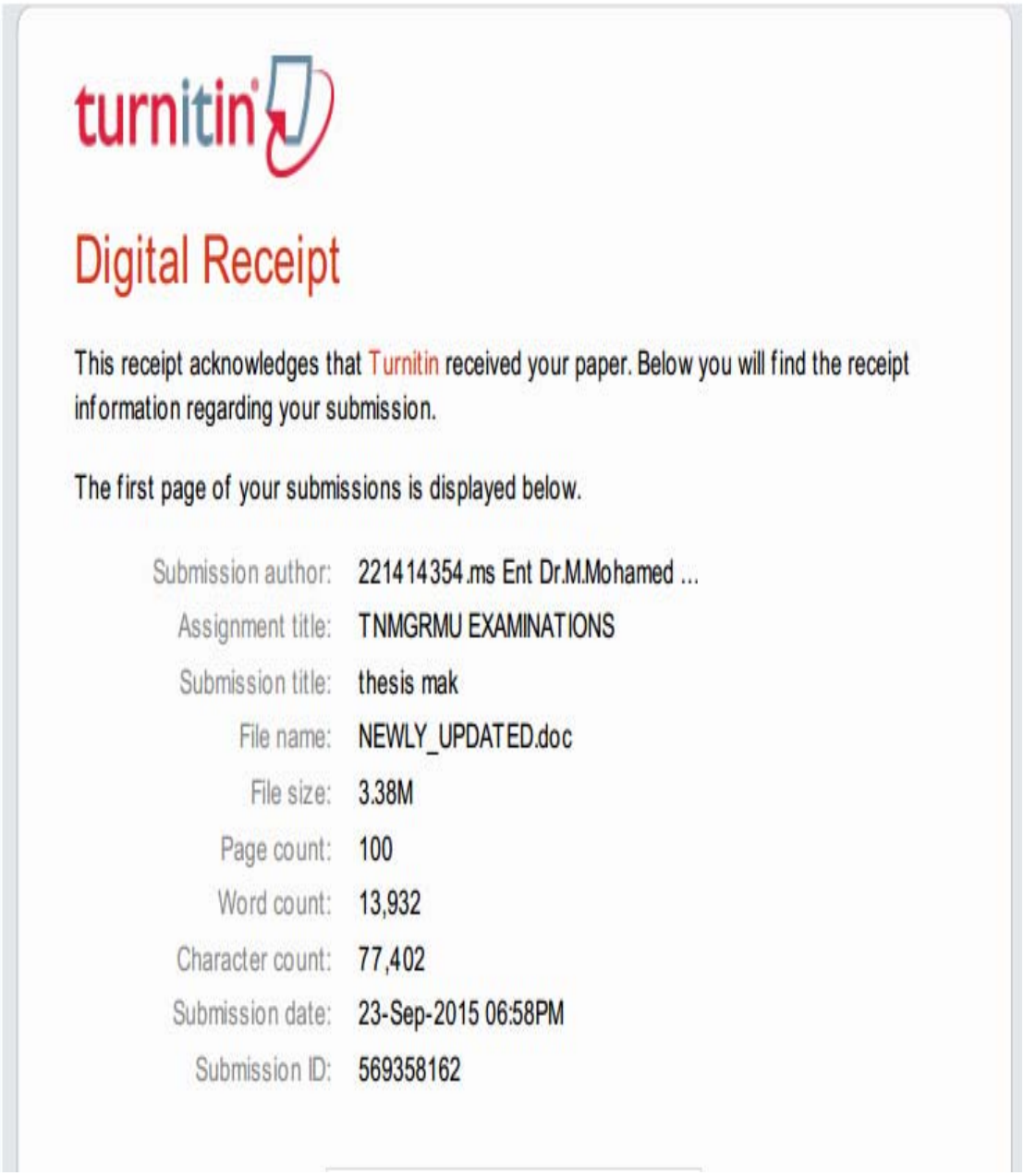

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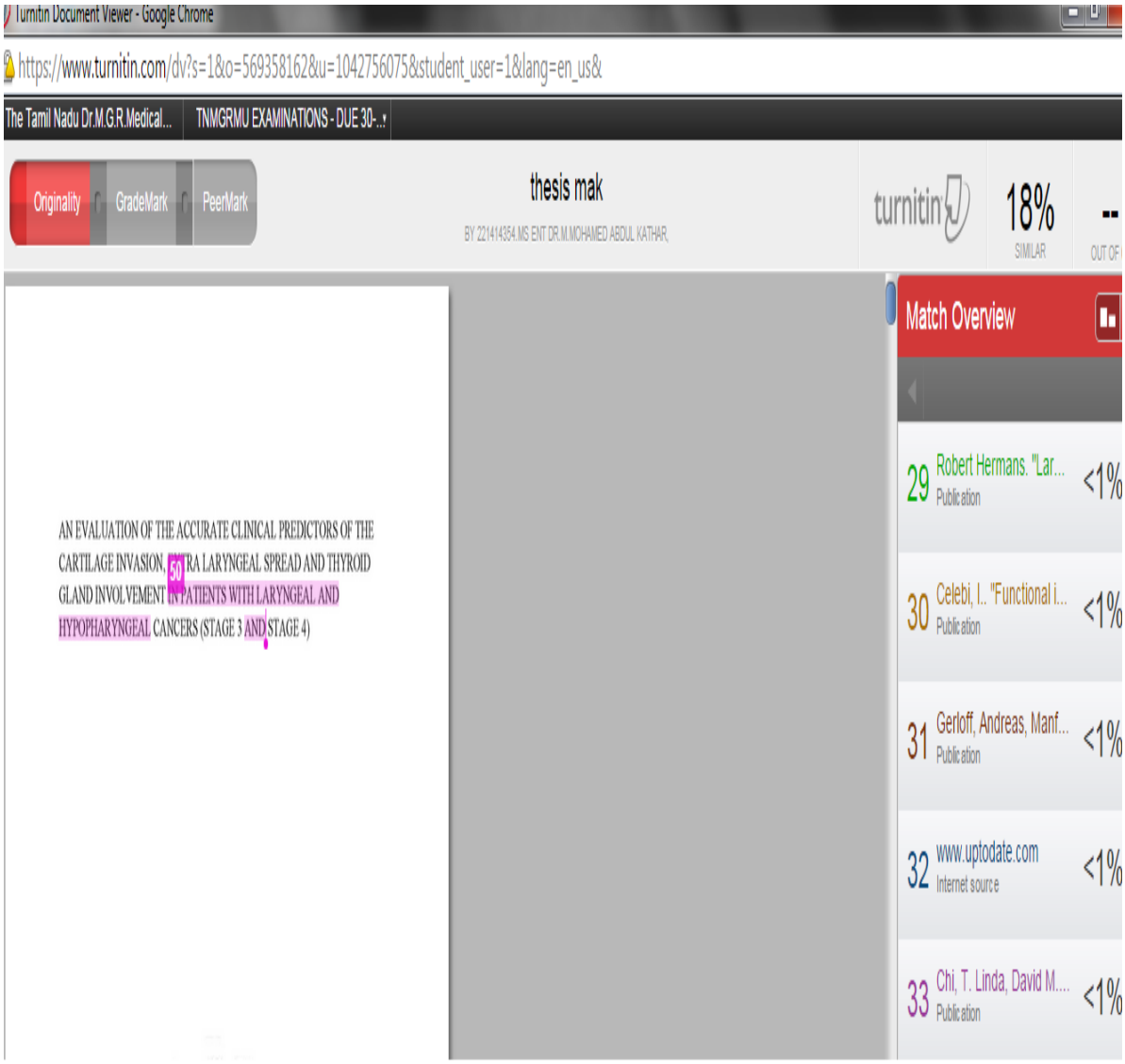
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Dr. M. Mohamed Abdul Kathar
PG Registrar
Department of ENT
Christian Medical College, Vellore 632 004

Sub: **Fluid Research Grant Project:**
An evaluation of the predictors of cartilage invasion (anterior commissure, lateral hypo pharyngeal wall and positive nodal status), extra-laryngeal spread and thyroid gland involvement in patients with laryngeal and hypo pharyngeal cancer. (Stage 3 and stage 4)
Dr. M. Mohamed Abdul Kathar, Dr. Rajiv Charles Michael, Dr. Anand Job, Dr. Rita Ruby Anbuselvi, Dr. Regi Thomas, ENT, Dr. Aparna Shyam, Radiology, Dr. Shramana, Dr. Veena Jeyaraj, Pathology, CMC, Vellore.

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Christian Medical College, Vellore - 632 002.

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Tel : 0416 - 2284294, 2284202 Fax : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

ACKNOWLEDGEMENTS

I wish to express my deep gratitude to Dr Rajiv Charles Michael, Professor and Head Of Unit 1, Department of Otorhinolaryngology, Speech and Hearing, Christian Medical College and Hospital, Vellore for his able guidance and encouragement in Conducting this study and preparing this dissertation.

I am grateful to Dr John Mathew, Head of the Department of Otorhinolaryngology, Speech and Hearing, Christian Medical College and Hospital, Vellore for his supportand encouragement in carrying out this study.

I would like to thank Dr. Rita Ruby Anbuselvi Albert from the Department of Otorhinolaryngology and I am extremely thankful to Dr.Regi Thomas from the Department of Otorhinolaryngology for their valuable advice and help.

I am extremely thankful to Dr. Sramana Mukopadhya and Dr.Veena jeyaraj from the Department of Pathology, Dr. Aparna shyam, Department of Radiology for their guidance in this study. I am also extremely thankful to all my friends and colleagues from the Department of Otorhinolaryngology for helping me in collecting the cases and for their help in making this study a reality.

I wish to thank Dr.Antoni samy, Head of the department, Department of Biostatistics for patiently analyzing the data and formatting it. Last, but not the least, a special thanks to my family, especially my wife Dr. Shajitha Begam for supporting me throughout the work on this study.

CONTENTS

INTRODUCTION

Laryngeal malignancy is the second common malignancy of the upper aero digestive tract, the first being malignancies arising from theoral cavity[1].90% of these malignancies arise from the epithelial lining of the larynx and hence are histologically squamous cell tumours. These carcinomas commonly affect the glottis. They can also develop from various premalignant lesions of the larynx. Early detection and treatment of laryngeal cancer is of paramount importance[1].Howeverit is very difficult to diagnose accurately access and diagnose invasive lesions on clinical examination. Imaging modalities such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) help in accurately determining the extent of the primary lesion which in turn aids in the staging and there by play a big role in planning treatment options for the patient[2].

Various studies in surgical histopathology by serial sectioning of laryngectomy specimen haveimproved the understanding of biological behaviour ofcancer and pathways of spread of laryngeal and hypopharyngeal cancer[1,2]. Advances in the imaging technology by Computerised Tomography scanning and Magnetic resonance imaging scanning have contributed further to the success of the voice conservation procedures by accurately determining the extent of the primary tumour.The success of organ preservation protocol is by accurately determining the depth of lesion; andimaging helpsgauge the depth of tumour, cartilage invasion and extra laryngeal

spread.The ability to achieve uniform dose curves has made radiation therapy a safe undertaking for early lesions of the anterior commissure[1,2].For more advancedlesions and large volume disease, where radiation therapy had only limited success, trials with hyper fractionated treatment to achieve better control rates are progressing.The comparison of different modalities of treatment ispossible with internationally accepted TNM staging by AJCC and UICC has its own fallacies,however it is an evolving system[1,2].

The proposed research is a prospective and retrospective study aimed at evaluating the clinical predictors of cartilage invasion, extra laryngeal spread and thyroid gland involvement in laryngeal and hypopharyngeal cancers. All patients presenting to the ENT OPDof Christian medical college are routinely evaluated clinically by a complete ENT and head and neck examination including indirect laryngoscopy and fibreoptic nasopharyngo- laryngoscopy. All clinically diagnosed patients with T3 and T4 lesions are subjected to a contrast enhanced CT scan (from skull base to mediastinum) as a standard protocol of management. Those patients with doubtful cartilage invasion are subjected to do limited MRI cuts(3 tesla MRI axial cuts STIR sequence done through the larynx).They are then planned for the direct laryngoscopy and biopsy. Biopsy proven laryngeal malignances (T3 and T4 with cartilage erosion and extra laryngeal spread) are advised to undergo total laryngectomy and tissue routinely sent for histopathology. All total laryngectomy and concomitant neck dissection specimens will be subject to histopathological study to evaluate cartilage invasion, extralaryngeal spread and thyroid gland involvement.

AIMS & OBJECTIVES

AIM

To evaluate the clinical predictors of cartilage invasion and extra laryngeal spread and thyroid gland involvement in patients with laryngeal and hypo pharyngeal cancers (stage 3 and stage 4).

OBJECTIVES:

1. To evaluate the accuracy of contrast enhanced Computed tomography(CECT and 3 Tesla Magnetic resonance imaging MRI STIR sequence axial cuts) in predicting cartilage invasion and extra laryngeal spread in patients with advanced laryngeal and hypo pharyngeal cancer(Stage 3 and 4) undergoing total laryngectomy.

2. To evaluate involvement of thyroid gland in patients undergoing total laryngectomy.

REVIEW OF LITERATURE

Laryngeal cancer is the second common cancerof the upper aerodigestive tractaccounting for approximately 25% of all head and neck cancers[1]. The incidence of laryngeal cancer in UK is approximately 4 per 1, 00,000 population. 70% occur in men with a peak incidence in the age group 55-65 years[1]. Males are predominantly affected with a female ratio of 2:1 in Scotland and 9:1in France. Geographically this disease was found to be widely distributed in Brazil, Afro-Caribbean population, France, Italy, India and Switzerland. Laryngeal cancer is seen to be more common in lower socio-economic group[1]. Few studies suggest that individuals residing in urban cities had a higher incidence than those residing in rural areas[2]. The glottis is the predominant site of involvement followed by the supraglottic region and 90-95% is histologically squamous cell carcinoma[1,2].

Squamous cell carcinoma are histologically characterised by

1. Individual cell keratinisation,

2. Inter cellular bridge formation,

3. Keratin pearl formation.

4. Increased nuclear cytoplasmic ratio

Smoking and alcohol consumption were found to have a synergistic effect on the development of squamous cell carcinoma[3]. The various theories postulated for development of laryngeal malignancies and habituation to alcohol was:

1. The constituents in the alcohol such as Quercetin (a naturally occurring flavonoid present in a variety of plants) and Rutin (the glycosidic form of quercetin and is one of the flavonoidsmost abundantly consumed in food) were also found to have carcinogenicpotential[3].
2. Acetaldehyde, a metabolite of ethanol cause more localized damage on cells.
3. Chronic alcohol use up regulatesthe Cytochrome P450 enzyme system thus converting procarcinogen to carcinogen.
4. It also affects the DNA repair enzymesresulting in increased chromosomal damage.
5. Alcohol profoundly reduces the T -helper cell number, thereby decreasing mitogenic activity and impairing macrophage activity.
6. A rich calorie in alcoholic beverages suppresses the appetite and metabolismleading to nutritional deficiencies and lowered resistance to cancer.

However tobacco acts via polycyclic aromatic hydrocarbons, like benzopyrene, whose products bind directly to DNA and RNA causing mutations[4]. Smokers are found to have a higher incidence of mutation of the p53 suppressor gene in head and neck cancer as when compared to non – smokers which can be explained by the carcinogenic activity of benzopyrene[4]. It is suggested that though various contents in alcohol are carcinogenic, it also acts as a solvent and increases the permeability of tobacco carcinogen in the upper aero-digestive tract increasing the risk of developing cancer by acting synergistically[3,4]. Other factor implicated is a genetic etiology as patients of laryngeal malignancies gives family history of malignancies.

New area of interest is in the role of Human papilloma virus infection in development of glottic cancers especially in the young non- smokers.

Squamous cell carcinoma predominantly affectsmale in the seventh decade.Most of these individuals belong to poor socioeconomic status. Smoking and alcohol consumption were found to have a synergistic effect on the incidence of development of squamous cell carcinoma[(4)].

ANATOMY OF LARYNX

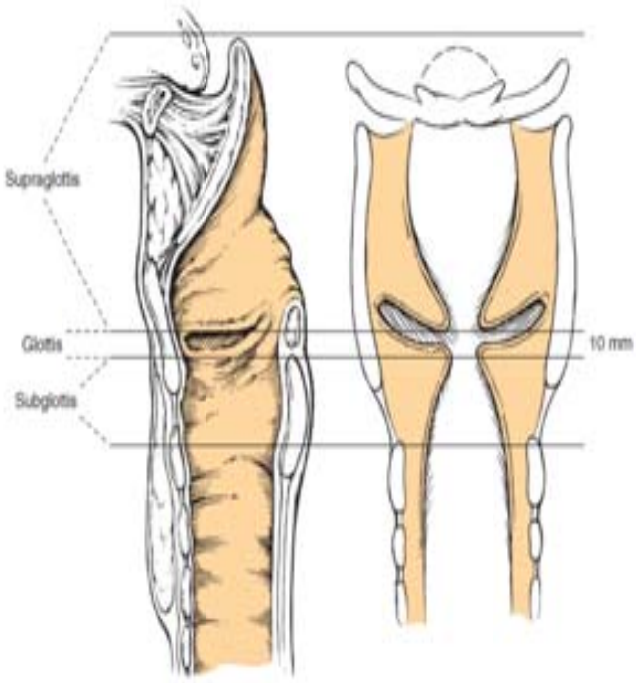


Fig.1 shows anatomy of various sub sites of larynx

ANATOMY:

Larynx also commonly referred to as voice box is divided in to three distinct sites which are further divided into different subsites[5]

1. Supraglottis: The supraglottis comprises

a. Suprahyoid epiglottis

- including tip, lingual or laryngeal aspect of epiglottis
- Aryepiglottic fold, laryngeal aspect
- arytenoids

b. Infra-hyoid epiglottis

c.ventricular bands or false cords

2. Glottis:

- vocal cords
- Anterior commissure
- Anterior commissure lies between the thyroid notch and the lower border of thyroid cartilage in male and upper one- third and lower two third of thyroid cartilage in female. [5]
- Posterior commissure

3. Subglottis

This consists of a mobile part from immediately below the true vocal cords to upper border of cricoid cartilage and a fixed part extends up to the inferior border of the cricoid cartilage.

Functions of larynx:

1. The primary function of the larynx is to protect the lower airway during swallowing.

2.Provides a stable fulcrum for the upper limbs.

3. Expectoration is expelled from the airway by cough reflex. It is preceded by for forceful inspiration,followed by rapid closure of both the vocal and vestibular folds. Air pressure is then built up below the adducted vocal cords as thediaphragm ascends until the vocal folds separate and mucus is expelled. [6]

4. Phonation.

The Larynx also contains several potential spaces which are important in spread of diseases.

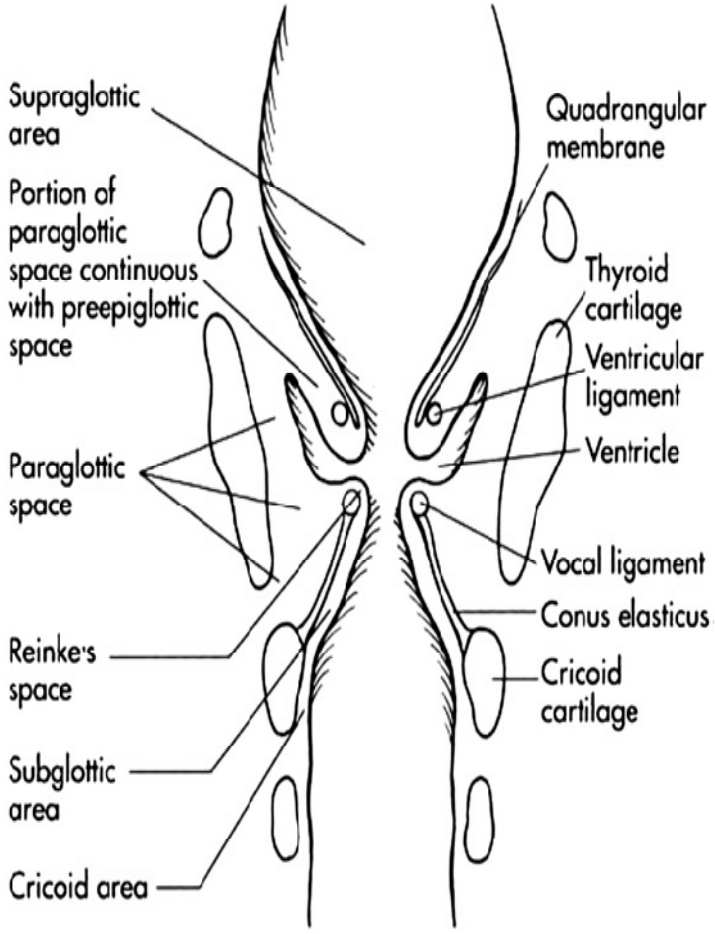


Fig.2: Figure showing the potential spaces of the larynx

These include:

Reinke's space:

Vocalcords consist of five layers histologically. They are

1) Outer squamous epithelial layer

2)Superficial layer

3) Intermediatelayer

4) Deep layer of lamina propria and vocalis muscle.

There lies a layer of loose tissue fibre and matrix between the outer squamous layer and superficial lamina propria layer.This region is called the Reinke's space.

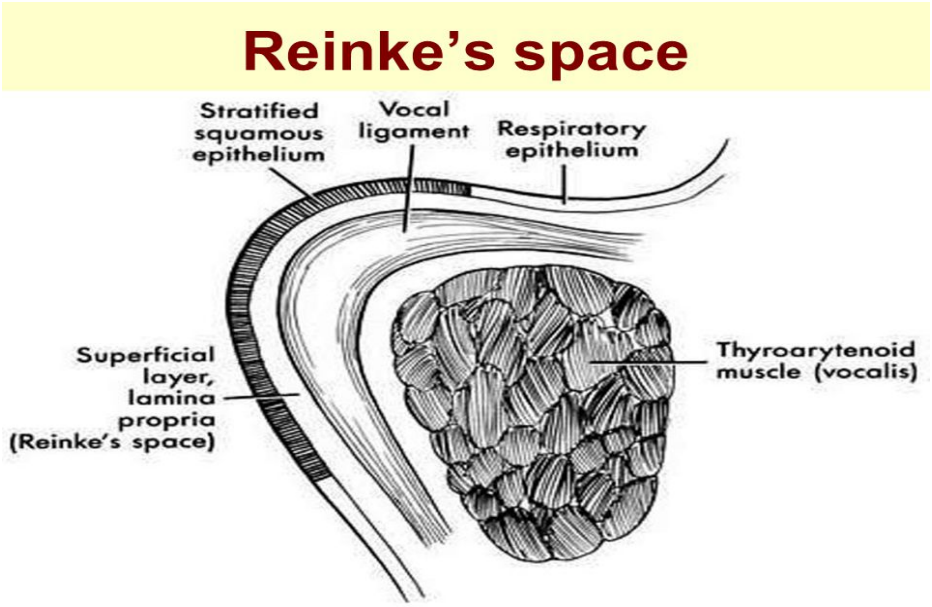


Figure 3: Figure showing the various layers of the vocal fold and Reinke's space

Pre epiglottic space of boyer

This **space** is bounded by the hyo-epiglotticsuperiorly,anteriorly by the thyrohyoid membraneandepiglottisposteriorlyand inferiorly by the thyro-epiglottic ligament.The epiglottis has cribriform areas that allow the spread of tumour from larynx to pre epiglottic space[5,6].

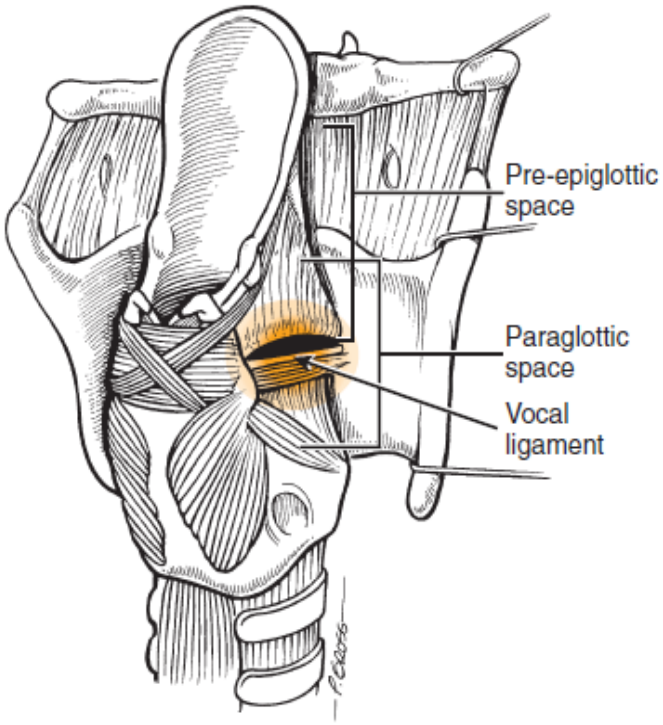


Fig.4: showing the pre-epiglottic spacer of Boyer and paraglottic space

Paraglottic space:

It is a spacewhich is bounded laterally by the thyroid cartilage anteriorly and mucosa of medial wall of pyriform sinus posteriorly. Superomedially by quadrangular membraneandinfero-medially by conus elasticus. [6]

Anterior subglottic wedge:

It is a triangular shaped zone with an apex terminating just below the anterior commissure tendon and which is delineated inferiorly by anterior arch of the cricoid. Anterior commissure tumours commonly spread in a mushroom like manner to involve this area and involve the cricothyroid ligament.

LARYNGEAL CARTILAGES:

There are three unpaired laryngeal cartilages:

- Thyroid cartilage(Largest cartilage in the larynx),
- Cricoid cartilage(complete ring),
- Epiglottis.

The thyroid and cricoid are hyaline cartilages; the epiglottis is an elasticcartilage

The Thyroid Cartilage:

The largest and important cartilagein the larynx is thyroidcartilage which acts as a protective layer to the mucosa of larynx[6].It forms the anterior and most of lateral walls of the larynx.The thyroid cartilage isincomplete posteriorly.The anteriorsurface

of this cartilage has a thick ridge, the laryngeal prominence.Thyroid ridge is easily seen and felt and it is commonly called the Adam's apple[6].During development, thyroid cartilage is formed by two segments of cartilage which meet in the midline to form the laryngeal prominence.The inferior border of the thyroid cartilage articulates with the cricoid cartilage; thesuperior surface has attachments to the epiglottis and smaller laryngeal cartilages like arytenoids.

The Cricoid Cartilage

Cricoid means signet- shape ("ring-shaped") cartilage**.** It is the only cartilage which formsa complete ring, the posterior portion of which is expandedto providesupport in the absence of a thyroid cartilage[6].The anterior portion iscalled anarch andthe posterior portionis alamina.The thyroid and cricoid cartilages protect the vocal cords and the entrance to the trachea,and the cartilage surfaces provide sites for the attachment of muscles and ligaments.Ligaments attach from the inferior surface of the cricoid cartilage to the first tracheal cartilage. The superior surface of the cricoid cartilage articulates with a pair ofarytenoidcartilages.

The Epiglottis

The horse shoe-shaped epiglottis projects above the glottis. The epiglottic cartilage has attachments to the anterior and superior borders of the thyroid cartilage and the hyoid bone[7].During swallowing, the larynx is raised, and the epiglottis falls back over the glottis, preventing the penetration of liquids or solid food into the respiratory airway.

The Three Paired Cartilages

The arytenoid cartilages articulate with the cricoid cartilage. The corniculate cartilages articulate with arytenoid cartilage.The arytenoidand corniculate cartilages play an important role in abduction and adduction of the glottis and production of sound. Thecuneiform “wedge-shaped” cartilages extendbetween the lateral aspect of arytenoid cartilage and the epiglottis.

LARYNGEAL LIGAMENTS:

Intrinsic ligaments bind all nine cartilages together to form the larynx.Extrinsic ligaments of larynx attach from the thyroid cartilage to hyoid and cricoid cartilage to trachea respectively[7]. The vestibular and vocal ligament extends between the thyroid cartilage andthe arytenoids. The vestibular ligaments and vocal ligaments are covered by folds of epithelium that project into the glottic region. The vestibular ligaments lie within the superior pair of folds, called as vestibular folds. These are inelastic, which help prevent foreign objects from entering the glottis.The vocal cords are highly elastic, because the vocal ligament is an elastic tissue. The vocal folds are involved in the production of sounds by adduction, and they are known as the true vocal cords. The vestibular folds play no part in production of sound and referred as the false vocal cord[7, 8].

THE LARYNGEAL MUSCULATURE:

The larynx musculature is divided into the intrinsic laryngealmuscles and the extrinsic muscles. The intrinsic laryngeal muscles have two main functions:

One set of musclestensesthe vocal folds and other set helps in open and close the glottis. Muscles that are involved with the vocal folds insert upon the thyroid, arytenoid, and corniculate cartilages[8]. Opening or closing the glottis involvesmovements of the arytenoids that move the vocal folds apart or together.

Extrinsic Laryngeal muscles

These musculatures position and stabilize the larynx and are called strap muscles of the neck. Three of the four strap muscles are sternohyoid, thyrohyoid, the omohyoidfind their attachment to larynx, however the sternothyroid is the only muscle failing to gain it[7,8].

BLOOD SUPPLY:

The superior and inferior laryngeal artery from superior and inferior thyroid artery accompanies the internal and recurrent laryngeal nerves respectively to supply the larynx.

NERVE SUPPLY:

The vagus nerve carries both sensory and motor innervations to the larynx.The sensory supply in the supraglottic region is carried by the internal laryngeal branch of the vagus nerve whereas the the vocal cords and the subglottic region are innervated by the recurrent laryngeal nerve.

All intrinsic muscles are supplied by the recurrent laryngeal nerve, except cricothyroid muscle,supplied by the external laryngeal nerve. The cricothyroid muscle tenses the vocal folds[8].

ANATOMY OF HYPOPHARYNX:

Hypopharynx is the region of pharynx that extends from the oropharynx superiorly tothe cervical esophagus inferiorly[9].The superior extent of hypopharynx is approximately at the level of hyoid bone.Inferiorly the hypopharynx tapers to the esophagus at the cricopharyngeus muscle.Hypopharynx is subdivided in to three regions:

- Pyriform sinuses
- Post cricoid region
- Posterior pharyngeal wall.

Pyriform fossa

Pyriform sinuses are present one on each side of the larynx. It is an inverted pyramid.Shallow above and deep below.It has medial, anteriorand lateral walls.Base of the pyramid at the level of pharyngo-epiglottic fold and apex extending just below the cricoid cartilage.[9]

- Medially bounded by aryepiglottic fold
- Laterally bounded by thyroid cartilage.
- Medial pyriform mucosa forms the posterior wall of paraglottic space.
- It is separated from endolarynx by aryepiglottic folds and lateral cricoarytenoidmuscle.

POSTERIOR HYPOPHARYNGEAL WALL

It extends from the level of hyoid bone to superior aspect of cricopharyngeus muscle.The posterior hypopharyngeal wall is separated from vertebral and paravertebral structures by a potential space- the retropharyngeal space.Tumours can easily cross this space to invade prevertebral tissue

POST CRICOID REGION

Post cricoid region is the anterior wall of hypopharynx extending from just below theposterior aspect of arytenoid cartilage to the esophageal introitus.Cancers commonly invades cricoid and posterior cricoarytenoid muscle; the only abductor of vocal folds causing early fixity of vocal cords. Its medial location to the tracheoesophageal groove can result in tumors involving the recurrent laryngeal nerve, delphian and thyroid gland[(9)].

EMBRYOLOGY:

The supraglottic region of larynx is derived from the buccopharyngeal anlage (arches III and IV).Glottic and subglottic portions are derived from the pulmonary anlage(arch VI)[(10)]. Each component has an independent lymphatic circulation, separated into an upper and lower drainage system.[(11)]

FUNCTIONS OF LARYNX

The different functions of the larynx are:

1. To protect the lower airway during swallowing[12]

2. Provides a stable fulcrum for the upper limbs.

3. Expectoration is expelled from the airway by cough reflex.

It is preceded by forceful inspiration, followed by rapid closure of both the vocal and vestibular folds. Air pressure is then built up below the adducted vocal cords as the diaphragm ascends until the vocal folds separate and mucus is expelled[12]

4. Phonation.

Thyroid gland Anatomy:

Thyroid gland means shield-like is situated in the midline of front and sides of neck. It regulates the basal metabolic rate, stimulates pyschic and somatic growth. It regulates calcium metabolism[13].Thyroid gland has right and left lobe connected by a small lobe called pyramidal lobe, Lalouette's pyramid.On the tracheal rings 2, 3, 4 lies the isthmus ofthe thyroid gland. Pyramidal lobe projectsfrom the upper border of the isthmus[13]. On eachside of isthmus are the lateral lobes of the gland.

The gland lies against vertebrae C5, C6,C7 and Tl, embracing the upper part of the trachea.Each lobe measures about 5 cm x 2.5 cm x 2.5 cm,and the isthmus 1.2 cm x 1.2 cm. On an average thegland weighs about 25 grams. [13]

a)Each lobe extends from the middle of the thyroidcartilage to the fourth or fifth tracheal ring.

(b)The isthmus extends from the second to thefourth tracheal ring.

Blood supply:

The thyroid gland is supplied by the superior thyroid arteries, a branch of external carotid and inferior thyroid artery, a branch of thyrocervical trunk.[14]

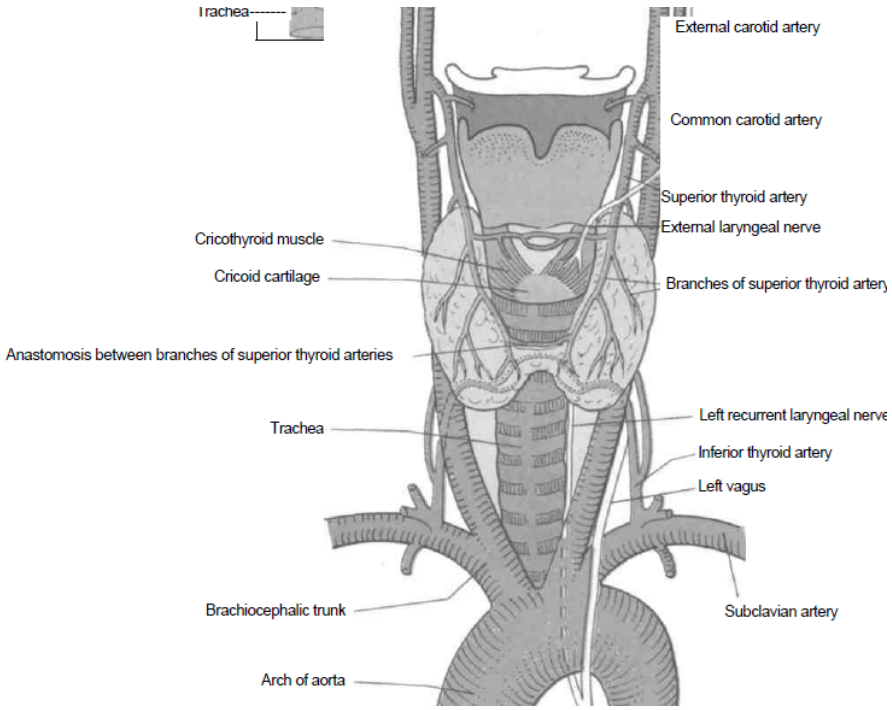


Figure 5.showing Anatomy of the thyroid gland

Venous Drainage

The thyroid gland is drained by the superior thyroid vein,middle and inferior thyroid veins.A fourth thyroid vein(of Kocher) may emerge between the middle and inferior veins, and drain into the internal jugular vein.

Lymphatic drainage

Lymph from the upper part of the gland reaches the upper deep cervical lymph nodes either directly or through the prelaryngeal nodes[14]. Lymph from the lower part of the gland drains to the lower deep cervical nodes directly, and also through the pretracheal and paratracheal nodes.

Nerve Supply

Nerves are derived mainly from the middle cervical ganglion and partly also from the superior and inferior cervical ganglion[13,14].These are vasoconstrictors.Joll's(Sterno-thyro-laryngeal triangle):Laterally: Upper pole of the gland and vessels

Superiorly: Strap muscles and deep investing layer of fascia to the thyroid.

Medially: Midline

Beahr's triangle:Recurrent laryngeal nerve lies in the third side of triangle.Other side of triangle are formed by inferior thyroid artery and common carotid artery.

Thyroid gland may be infiltrated in laryngeal cancers by direct invasion. Nowadays total laryngectomy id performed in all advanced operable cancers or as salvage surgery after failure of organ preservation protocol and frequency of thyroidectomy

along with the total laryngectomy is also reduced due to low reported frequency of thyroid gland involvement by tumour cells. 11% percent to 43% of patients with total laryngectomy and radiotherapy will results in hypothyroidism and the risks raises to 48% to 100% when it is associated with hemithyroidectomy[13].Indication for thyroidectomy during total laryngectomy is the subject of medical debate.

Our study helps us to identify whether thyroidectomy is really indicated with total laryngectomy or not to avoid long term side effects following surgery or combined modality of treatment. Nowadays the routine protocol of management is either hemithyroidectomy or total thyroidectomy.In 1955, Ogura published a series of 59 patients with laryngeal cancer, of whom 10% had thyroid gland involvement. Based on the proportion, he recommended that ipsilateral thyroid gland removal will be routine carried out in all total laryngectomies. Pre-operative CT scans also failed to categorize patients according to their thyroid gland status. Failure to demonstrate thyroid gland involvement in CT scans was also noted by Elliott et al. Similar proportions of cartilage invasion were found in patients with and without thyroid gland invasion. [14]

LYMPHATIC DRAINAGE AND NODAL METASTASIS OF LARYNX

Lymphatics from the supraglottis exit the larynx through thyrohyoid membrane alongside the superior laryngeal vessels in to the jugulo-digastric nodes.

The lymphatics of the true vocal cords are sparse. Lymphatics from the glottis and subglottis pass through the cricothyroid ligamentand drain in to the prelaryngeal

node,Delphiannode, paratrachealnodes and the deep cervical nodes along the inferior thyroid artery**.**

With a single level of lymph node involved by metastatic disease, the prognosis is said to be reduced by half. Criteria that suggest metastatic involvement of a lymph node. The sensitivity of CT and MRI in detecting nodal metastasis is higher than Clinical examination. Unfortunately, the negative predictivevalue of imaging (CT scan or MRI), is not sufficiently high to reassure the surgeonand avoid neck dissection. Decision regarding neck dissection in lesions stagedas N0 (by CT scan and clinical examination) depend on the presumed risk for nodal metastasis and the comfort level of the surgeon and patient. The risk for nodal metastasis can be determined on the basis of the site, depth, and extent of the primary tumour. Extranodal extension predicts a worse outcome independent of the N-grading score. For glottic cancer, large tumour volume, anterior commissure involvement,ventricle involvement, and cartilage involvement are associated with high rateof failure. The only independent risk factor that is consistent with studies is cartilage invasion, which is identified by CT as inner cortex irregularity and by MRI as signal change. Another study classified glottic tumors as being adjacent to and away from thethyroid cartilage inner cortex and demonstrates a worse local control rate for the lesions that contact the cartilage independent of the status of cortical irregularity. Node includes enlarged size, abnormal shape, central necrosis, peripheral rim enhancement and extracapsular spread.

PATTERNS OF GROWTH AND SPREAD OF LARYNGEAL CANCER:

Growth and spread is largely determined by site of origin of the primary lesion. The main factors determining the spread and extension of tumour growth are anatomic barriers produced by the laryngeal compartments[15].Glottis develops from the paired structure that fuses in midline. At the anterior commissure, where these structures meet, the anterior commissural tendon forms a barrier to spread from one vocal cord to another vocal cord[15]. There is no such midline barrier in the supraglottis and subglottis,thus circumferential spread is not restricted in these regions.The conus elasticus is a tough fibro-elastic membrane extending from the upper margin of cricoid cartilage to the free margin of the vocal cord. This acts as a barrier to spread from glottis tosubglottis.The quadrangular membrane acts as a supraglottic barrier.Invasion of cartilage usually occurs in areas of ossification but may occasionally occur in unossified cartilage.

Supraglottic tumours:

Supraglottic tumours spread in an upward direction towards the base of the base of the tongue and rarely involve the larynx below the ventricle. This unique pattern of tumour spread renders these tumours suitable for the supraglottic partial laryngectomy[15]. Cancers within each subsite of the supraglottis are distinct in terms of tumour spread and management.

Epiglottic tumours:

Clinically the epiglottis is divided into a suprahyoid and an infrahyoidpart, with reference to the level of the hyoid bone. Tumours are proliferative masses with

minimal underlying invasion; these tumours tend to be overstaged because of their size and ball- valve like obstruction of the airway[15]. If the base or pedicle is narrow they are eminently suitable for endoscopic laser excision.Tumours of the infrahyoid epiglottis are usually deeply infiltrative in nature. Infrahyoid epiglottic lesions may also grow circumferentially to involve the false cords,Aryepiglottic fold. Pre epiglottic space involvement occurs. Bulky pre – epiglottic space masses undergo central necrosis due to a relative lack of blood supply and generally respond poorly to radiotherapy.Epiglottic tumours rarely invade the thyroid cartilage. Hence, the perichondrium on the superior border of the thyroid cartilage may be safely elevated while performing a supraglottic laryngectomy. Thyroid cartilage invasion occurs late and implies transglottic spread which is an absolute contraindication to supraglottic laryngectomy.

Tumours of the false cord

Cancer of the false cord or ventricular fold was relatively uncommon[16]. Tumours from this region spread upwards to involve theepiglottis. Posteriorly it mayinvolve the aryepiglottic fold and arytenoids and inferiorly the anterior commissure. The anterior commissure acts as a barrier to inferior spread[16]. If this is breached there is a high chance of thyroid involvement.

Tumours of the arytenoids and aryepiglottic fold

Lesions confined purely to the arytenoids and aryepiglottic fold are uncommon. Cancers in this area usually spill into the adjacent pyriform fossa or post cricoid[17].Early in the course of the disease they behave differently from other cancers in the supraglottic larynx and are more like pyriform fossa tumours. These lesions are common in India and are also referred to as marginal zone cancers.

Glottic tumours

Glottis lesions are a heterogeneous group of disorders rangingfrom a keratotic lesion, progressing through various grades of atypia (mild,moderate, severe) to an in-situ carcinoma and finally invasive cancer[17].In – situ carcinoma does not invade the basement membrane. Most glottis cancers arise in the free margin of the anterior two thirds of the vocal cord. Initial spread occurs horizontally towards the anterior commissure.Very early cancers are limited to the mucosa without involvement of the

underlying muscle because of reinke's space, as the anterior commissure is reached , a dense mass of fibro elastic tissue (thyroepiglottic ligament , conus elasticus and inner perinchondrium of the thyroid ala) prevent further spread Vertical spread of the tumour upstages it to T_2 and is usually subglottic. Inferior spread is limited by the conus elasticus which is a barrier between the glottis and sub glottis[17]. This tough membrane is weakest at point where neurovascular bundles enter or exit the larynx. Deep lateral invasion occurs in the paraglottic space with infiltration of the thyroarytenoid muscle[18].Very early cancers are limited to the mucosa without involvement of the underlying muscle because of reinke's space , as the anterior commissure is reached , a dense mass of fibro elastic tissue (thyroepiglottic ligament , conus elasticus and inner cortex of the thyroid cartilage) prevent further spread Vertical spread of the tumour upstages it to T_2 and is usually subglottic . Contiguous spread eventually leads to invasion of the ossified or calcified lower border of the thyroid ala and outside the larynx through the cricothyroid membrane into the strap muscles and thyroid gland. They commonly extend superiorly in to the false cord and aryepiglottic old (glottis carcinoma with supraglottic extension) .The degree of subglottic extension is vital in planning a conservative vertical hemilaryngectomy.The critical cut off level is limited to the cricoid cartilage which lies 10mm anteriorly and 5mm posteriorly. Primary posterior lesions of the glottis are rare; however the posterior commissure is frequently involved by advanced tumours from other sites. There is rapid invasion of the arytenoids, cricoarytenoid joint and cricoid cartilage. The paraglottic space is then invaded and tumour extends vertically downwards

towards the cricothyroid joint.Lateral spread occurs submucosally to involve the apex of the pyriform fossa.

Anterior commissure lesions

Primary tumours of the anterior commissure are uncommon. The anterior Commissure is usually involved by secondary spread when a membranous cord lesion extends across the midline[19]. The anterior commissure is directly attached to the thyroid cartilageby the broyle's tendon[19]. Early invasion of the cartilage is therefore common in these tumours. Tumour spread superiorly, involves the base of the epiglottis while inferiorly thetumourexitsthe glottis. Patients with lesions involving the anterior commissure were generally advised to undergo surgery due to fear of early cartilageinvasion and consequently poor radiotherapeutic response. However, the mass of fibro elastic tissue at the anterior commissure offers a dense barrier to the spread of early glotticcancer. It is now recognized that stage for the anterior commissure is not any more readily invaded than any other part of the larynx. The pattern of tumour growth at the anterior commissure indicates the propensity to invasion of the thyroid cartilage. If tumour extent from the vocal cord onto the lower portion of the epiglottis at the anterior commissure, the risk of thyroid cartilage invasion is extremely great [20].Glottic cancers crossing the anterior commissure onto the opposite cord can be treated with an extended hemilaryngectomy. This is feasible if at least one half of the remaining true cord can be preserved.

Subglottic tumours

Subglottic tumours are rare and account for less than one per cent of all laryngeal tumours. Tumour spread occurs bilaterally and along the entire circumference of the subglottis[21]. The cricoid cartilage is involved early because of the absence of an intervening muscle layer. Fixity of the true vocal cords is usually the presenting feature.

Transglottic tumour:

The term transglottic was first coined by McGavran. The tumour that crosses theventricle from supraglottis to glottis or sometimes the subglottis also. It does not imply the site of origin, but was meant to describe areas involved by the carcinoma. They are important because they usually present as advanced with the cartilage invasion, extralaryngeal spread or involvement of opposite side and therefore are treated by near total or more often, a total laryngectomy[22]. Tumors of supraglottis can occassionally become transglottic by spread onto the anterior commissure. These tumors are highly aggressive and invade cartilage early. Supra glottic or Glottic tumors with posterior extension become transglottic by spread on to the cricoarytenoid joint or inter arytenoid area[21,22]. Extra laryngeal spread occurs through the thyroid cartilage, the cricothyroid membrane or the thyrohyoid membrane.

Staging evolution

The modification of the AJCC TNM staging protocol occurred in the year 2002. Although this staging provides clear picture about prognosis, it does not

stratify the patients into the various treatment modalities to assist the clinicians. The American society of clinical oncology formed a multidisciplinary team. Regardless, the report did recommend that T1 and T2 cancers, the laryngeal function with should be preserved adopting a single treatment modality. For most T3 and T4 without cartilage invasion or penetration, an organ- preservation modality is an appropriate and standard treatment option. However, organ preservation protocol does not render a survival advantage in comparison to total Laryngectomy.

IMAGING ANATOMY OF LARYNX

Supraglottis

The supraglottic larynx is delimited inferiorly by the superior surfaceof the true vocal cords. On cross-section, the false vocal foldsare easily separated from the true cords by submucosal presence of fat inthe false vocal cords[23]. The pre-epiglottic space of boyer is filled with fat tissue. Rich lymphatic drainage to the high deep cervical chain contributes to the higher chance of incidence of node metastasis during the time of diagnosis of lesions in thisregion[23].

Glottis

The truevocal folds anterior commissure and posterior commissurecomprise the glottis. Radiologically, the vocal folds are differentiated from the false vocal cords by the presence of submucosal soft tissue density which attributes to the vocalis

muscle[23]. Lymphatic drainage from the glottis is very sparse. So there is rare chance of nodal metastasis from glottic cancer.

Subglottis

The endoluminal contour of the subglottis is normally smooth.The presence of subglottic soft tissue should raise suspicion of neoplasm. Lymphatic drainage from the subglottis is sparse, and nodal metastasisfrom lesions in the subglottis is rare.

Contrast enhanced CT scan of neck at the level of A)Supraglottis – submucosal fat plane at the level of supraglottis and short arrow denotes the arytenoids cartilage

B)Glottis - submucosal fat plane at the level of glottis because of thyroarytenoid muscle

c) Subglottis – no submucosal tissue in the subglottis at thelevel of the cricoid so that the air column abuts the cartilage

RADIOLOGICAL EVALUATION OF LARYNGEAL CANCER

Pre-epiglottic(Boyer's space) and paraglottic space spread

The pre-epiglottic space is readily identified on non contrast T1-weighted MRI or CT, particularly in the sagittal plane, because of its fat contents[23,24]. The pre-epiglottic space is continuous with the paraglottic space on either side. The para glottic space is present between the thyrohyoid membrane, thyroid and cricoid cartilages supero- laterally and infero-laterally respectively and between the false and true vocal cords and the elastic cone medially. It contains fat at the level of the false vocal cords. This can be easily identified on axial and sagittal non contrast T1-weighted MRI and CT, because fat tissue has unique imaging features. In a study conducted by Loevener et al, he concluded that breaching of the pre-epiglottic fat by glottic or supraglottic carcinomas is rather difficult to diagnose clinically but is often easily appreciated by a head and neck radiologist. It is seen as replacement of the normal fat on CT or MRI". [24]

Anterior and posterior commissures:

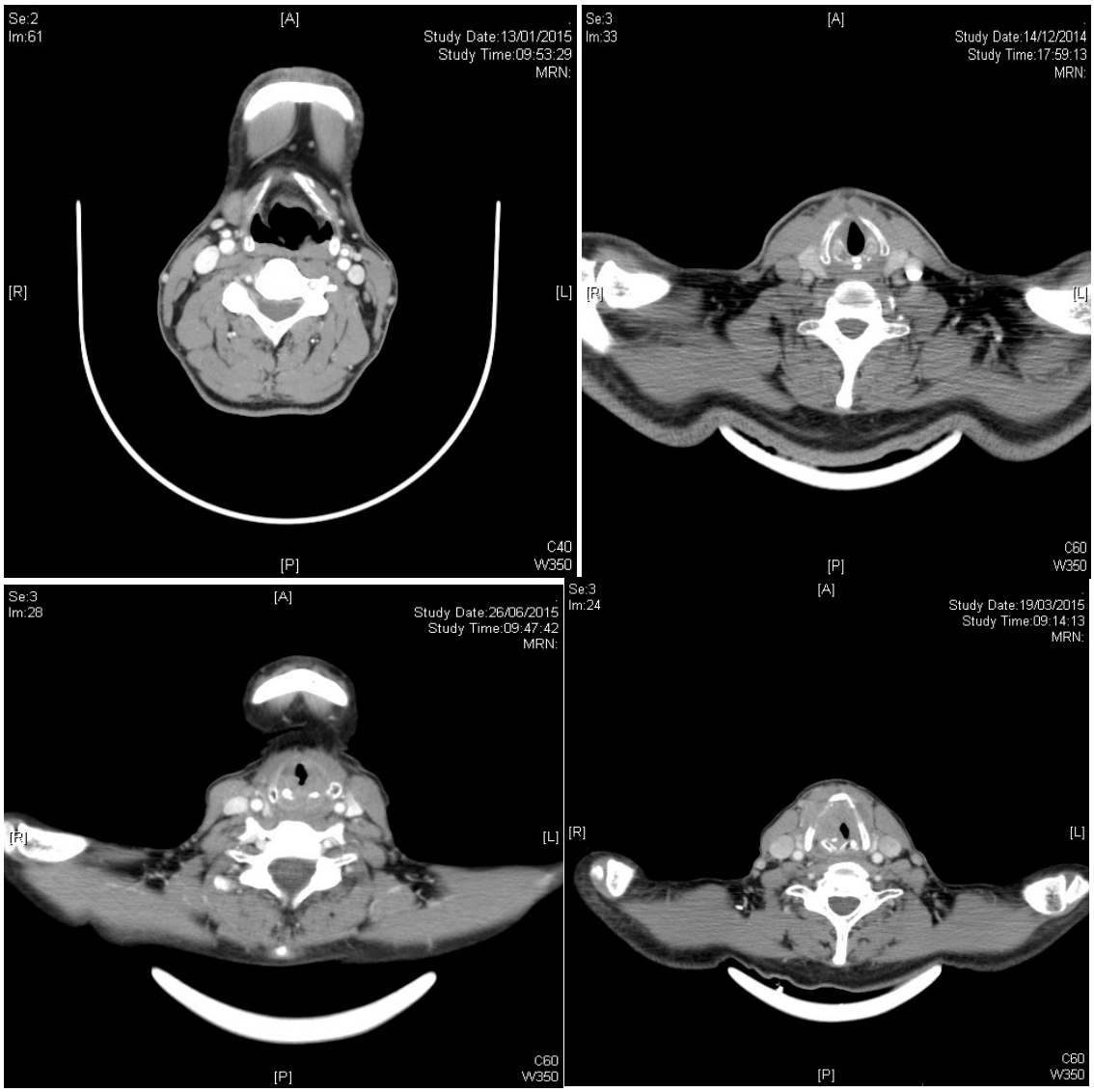
Between the meeting sites of the two vocal cords to the thyroid cartilage is a ''bare'' area, where the laryngeal mucosa abuts the thyroid cartilage[24]. The mucosa covering the posterior wall of the both vocal cords are known as the posterior commissure.When there is visible soft tissue in the region of the anterior or posterior

commissure, tumour infiltration is considered, although physiologic appearance of the vocal cords and edema can give similar appearance[24]. Simple bulging of the true vocal cordor ventricular band mass into these regions should not be overinterpreted as invasion. Endoscopic evaluation of the mucosal extent of disease in these commissures is more reliable than imaging, however, submucosal extent, particularly in the form of cartilage invasion or extension through the cricothyroidmembrane, is common once the anterior commissure is involved and often escapes clinical detection. Extension of a vocal cord growth to the anterior commissure does not change the TNM staging but may affect patient's survival and choice of treatment. If the posterior commissure is involved, then it is a contraindication for supracricoid partial laryngectomy[25].

Cartilaginous invasion

Cartilaginous invasion does not respond to radiationand therefore radiation in these patients'increases chances of radiationinduced-necrosis[25]. Therefore, cartilaginous invasion is an important criterionin assessing the modality of treatment to be adopted.Fortherapeutic decision making, the presence of cartilaginous invasion often justifies surgery that might not be undertaken otherwise. Because the cartilaginous structures are difficult to assess in clinical examination, assessment of the possibility of cartilaginous invasion before treatment is necessary by imaging.The characteristics of hyaline cartilage are variable in imaging[25]. Ossification of the cartilaginous structures of the larynx increases with age but varies[26,27]. Ossified cartilage demonstrates higher attenuation on CT at the outer and inner cortices with

relatively lower attenuation, nonossified cartilage demonstrates attenuation similar to that of other soft tissue. On MRI STIR sequence,the cortical signal depends on the presence or absence of calcification, andthe fatty medullary signal explains T1 hyperintensity with intermediatesignal on T2-weighted images. Reactive changes within cartilage may occur without the presence of invasion, resulting in overestimation of extent, particularly with MRI (32).Both CT and MRI technique should be able to aid in the differentiation of inner cortical invasion (T3) from involvement of inner and outer cortices and extralaryngeal spread (T4). MRI allows for excellent soft tissuecontrast and has been viewed as superior to CT scan for detection of cartilage invasion. MRI demonstrates increased T2 signal and low to intermediateT1 signal, with abnormal enhancement in cases of replacement orinfiltration of hyaline cartilage.The sensitivity of MRI and high negative predictive value, MRI is generally been preferred over CT at the time of initial evaluation. Becker and colleagues studied the CT evaluations of 111 patientsand describe CT signs with high specificity, including the presence of invasionor erosion (93% specificity) or extralaryngeal spread (95%specificity). Because these signs depend on relatively advanced disease,their sensitivity is understandably low. Conversely, the presence ofsclerosis within a cartilage is relatively sensitive, but the specificity of this sign varies with location. It was lower in the thyroid cartilage(40% specificity) when compared to cricoid and arytenoid cartilages (76%–79% specificity)(26).



High resolution contrast enhanced CT scan from skull base to mediastinum showing thyroid cartilage erosion, arytenoid cartilage and cricoid cartilage destruction.

Prevertebral region involvement

The prevertebral fascia involvement by tumour renders the tumour unresectable. Unfortunately, the determination of prevertebral involvement is best detected by intraoperative assessment of that region . Radiologic detection of prevertebral involvement is controversial. There is a small amount of fat tissue within the retropharyngeal space which can be identified on imaging like MRI and CT in most individuals.MRI gives the clear details than CT scan[32]. Absence of obliteration of this fat plane is indicator for lack of prevertebral involvement. Obliteration of the fat plane, does not reliably predictprevertebral involvement by the tumour unless obvious tumour bulk is present[33].

Carotid artery involvement

Extralaryngeal spread of tumour to infiltrate carotid artery renders the tumour inoperable. However, not all tumors abutting the carotid infiltrate the tunica adventitia. The determination of resectable from unresectable tumours relies heavily on imaging findings[33]. If tumour contacts more > 270 degree of the circumference of the carotid, the likelihood of invasion is high and these tumors are deemed unresectable. Contact less than 180 degree has a low chance of tumour invasion.

Role of MRI in laryngeal cancers:

CT scan neck from skull base to mediastinum is the routine investigation of choice for the management of choice for advanced laryngeal cancers (34). In 1976, CT scan has become the reliable investigation for evaluating the tumours of head and neck and is considered as the important for pre evaluation of laryngeal cancers. CT scan has its own limitations especially in determining the cartilage invasion due to irregular mix of calcified, ossified and non calcified cartilage. Cartilage invasion helps in judging which patients need voice preservation protocol and which patient needs laryngectomy.

Recently MRI(Magnetic resonance imaging) has proved to be a reliable diagnostic indicator in diagnosing the cartilage invasion. However it has still not been determined whether CT or MRI is the best predictor used in pre therapeutic evaluation of laryngeal cancers (35).

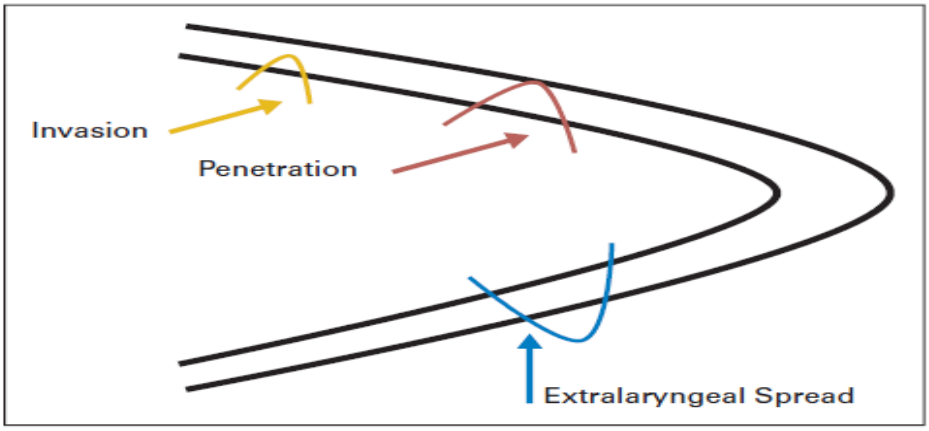
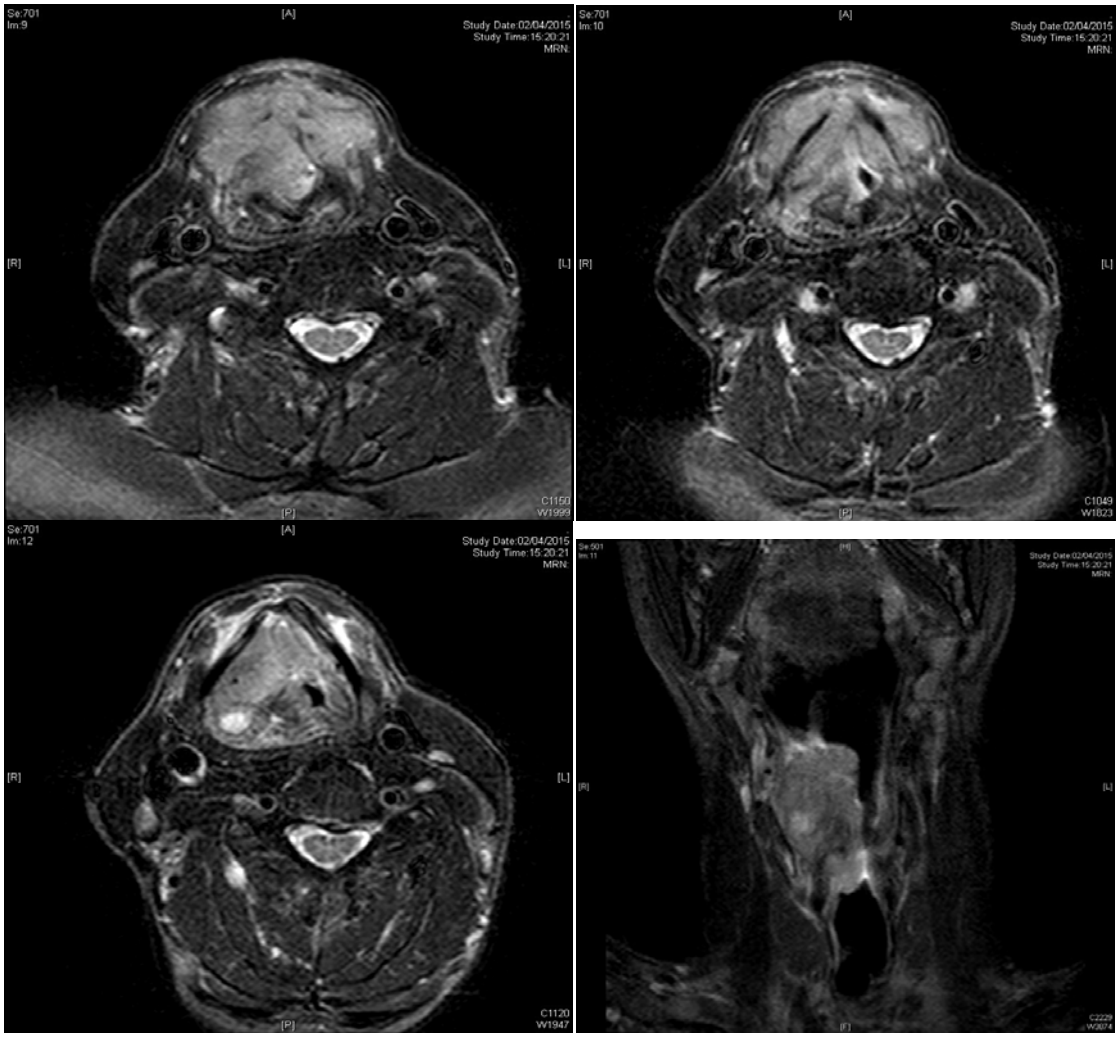


Diagram showing invasion, penetration and extralaryngeal spread in patients with laryngeal cancer in CT neck contrast from skull base to mediastinum.



3 Tesla MRI Limited STIR HR axial MRI sections were done through the larynx showed thyroid and arytenoid cartilage destruction.

PRIMARY AND SALVAGE TOTAL LARYNGECTOMY

The results of early laryngectomies of previous century were disastrous because of aspiration, pneumonia, hemorrhage, sepsis and pharyngo cutaneous and chylous fistula (neck dissection) formation. In 1892, Solis-Cohen devised the principle of suturing the trachea to the skin. Also in the late nineteenth century, Gluck and Sorensen added to theprinciple of divert trachea to the skin and introduced reconstruction of the neo- pharynx. Over time, not only has the procedure of TL been changed, but there is also an increasing emphasis on voice and swallowing preservation. In 1980, Singer and Blom introduced the tracheoesophageal Puncture (TEP) and prosthesis, for restore voice after Total Laryngectomy. The concept of organ preservation was introduced and partial laryngectomy procedures and chemoradiation protocols became the treatment of choice when Possible. In spite of all these advancements, TL still has a role in the treatment of patients who have advanced laryngeal cancer.

Indications

The indications for total laryngectomy have decreased as organ preservation strategieshad mandated a paradigm shift. Induction chemotherapywith cisplatin plus fluorouracil followed by radiation therapy allowedpreservation of the larynx in 64% of patients without affecting survival when compared with total laryngectomy (TL) and adjuvant radiotherapy. In 2003, Forestiere and colleagues showed that concurrent chemotherapy with cisplatin and radiotherapy resulted in high organ preservation

rates, good loco-regional control rate, and similar overall survival when compared with induction chemotherapy followed by radiation.

Primary Total laryngectomy

This procedure is indicated in advanced disease that is not amenable to partial laryngectomy, concurrent chemo radiation, or radiotherapy. Tumors that penetrate through cartilage, invade into the extralaryngeal soft tissue of the neck, and extensive involvement of the base of tongue are suitable for this procedure.

Non-neoplastic indications

Include laryngeal dysfunction with aspiration or chondro-radionecrosis of the larynx. Also, pulmonary status and medical comorbid illness and mental status may define the treatment options for a given patient.

Salvage Total laryngectomy

Indicated for chemoradiation, radiation, or partial laryngeal surgical failures. Salvage laryngectomy was required in 16% treated with concurrent Chemoradiation and 31% of patients treated with radiotherapy alone. Salvage total laryngectomy can be technically more difficult and carries a higher postoperative complication rate.

MANAGEMENT OF NECK

The larynx drains into levels 2 to 4 pretracheal and paratracheal lymphnodes within the neck. Advanced laryngeal cancers have an overall 30% of occult neck metastasis. Patients who have supraglottic and advanced glottic with clinically N0 neck should undergo elective treatment of the neck by either neck dissection or radiotherapy. Supraglottic tumors have a significant propensity for bilateral neck metastasis, and bilateral necks should be addressed. Patients with N1 disease who are treated with definitive chemo radiotherapy require a neck dissection in case of incomplete clinical response. Neck dissection arguably is required for patients with N2 or N3 disease who are treated with definitive chemo-radiotherapy. For salvage surgery, the decision to perform a neck dissection should be based on CT staging of the neck, as most patientswho are radiologically staged N0 are unlikely to harbour occult nodal disease.

MATERIALS AND METHODS

The purpose of this study is to identify the accurate clinical predictors of cartilage invasion, extra laryngeal spread and thyroid gland involvement in patients with laryngeal and hypopharyngeal cancers (Stage 3 and stage 4)

Type of study: Prospective and retrospective study

Period of study: 1 year period

Settings: This study was performed in the ENT outpatient department at the Christian medical college, Vellore between 2014 to 2016. All patients presenting to the ENT outpatient department with symptoms of change in voice, difficulty in swallowing, difficulty in breathing and neck swelling were evaluated clinically by a complete ENT and head and neck examination which included indirect laryngoscopy and fibreoptic laryngoscopy.

All clinically diagnosed patients with T3 and T4 lesions were subjected to do contrast enhanced CT scan (from skull base to mediastinum) as a standard protocol of management. Those patients with doubtful cartilage invasion were subjected to undergo limited MRI cuts (STIR sequence) of the neck. They were laterplanned for the direct laryngoscopy and biopsy.The biopsy proven laryngeal malignancies (T3 and T4 with cartilage erosion and extra laryngeal spread) were advised to undergo total laryngectomy with the post-op specimen sent for histopathology. These all total laryngectomy were subjected to histopathological evaluation were noted for cartilage invasion, extra laryngeal spread and thyroid gland involvement.

The aim of this study was to individually assess the accuracy of pre-operative CT scan, MRI and clinical/e ndoscopic staging of laryngeal cancers by comparing clinical findings,imaging andhistopathological findings.

ELIGIBILITY CRITERIA-

Inclusion criteria:

All patients with Laryngeal and hypo pharyngeal cancers(Stage 3 and stage 4) presenting to the ENT outpatient clinic planned for total laryngectomy with or without thyroidectomy and with or without neck dissection at Christian Medical College& Hospital between 2013 and 2015.

Exclusion Criteria:

1) Post laryngectomy recurrence,

2) Skin involvement and

3) Distant metastasis

Sample size calculation

A sample of 41 patients will be required to obtain a 95% confidence interval of ± 10% around a positive predictive value of 88% in CT scan.

$n= 4pq/d^2$

p=positive predictive value=88%

d=10%

Where,

n = sample size

P = sensitivity

Q = 100 – P

d = precision

Patients diagnosed clinically as laryngeal cancer are routinely sent for flexible Nasopharyngo laryngoscopy (Karl storz) to confirm the diagnosis and extension of the lesion. Contrast enhaced computed tomography is ordered as routine protocol of management in patients diagnosed with laryngeal cancer. Those patients in whom doubtful cartilage invasion were sent for limited cuts of MRI.We have done MRI sections on 3 T MRI. MRI limited cuts (limited STIR HR, short tau inversion recovery high resolution axial MRI sections were done through the larynx).

Patient's laryngectomy specimen is finally for sent for histopathological analysis to compare the findings with imaging.

Statistical methods:

From literature review data will be summarized with counts and percentages for categorical variables and mean and standard deviation for normally distributed continuous variables and median and range for non-normally distributed

continuous variables.chi square test will be used for comparing the proportions between the groups**.** Diagnostics summary measures (sensitivity, specificity, predictive values) will be obtained with 95% confidence limits.

Study population recruitment:

All patients presenting to the ENT outpatient department with symptoms like hoarseness of voice , dysphagia, breathing difficulty and neck swelling and fulfilling inclusion and exclusion criteria had complete ENT and head and neck examination, indirect laryngoscopy, Naso-pharyngo-laryngoscopy (NPL scopy) using flexible laryngoscope (Karl Storz, Germany)., CT neck with contrast from skull base to mediastinum and subjected to do MRI limited axial cuts (STIR sequence) where done through the larynx, if there is doubt in cartilage invasion and they were planned for microlaryngoscopic examination and biopsy surgery under general anaesthesia. Patients with histopathologically proved cancer were subjected to Total laryngectomy and specimen were finally analysed and compared with imaging.

PROCEDURE:

Patients diagnosed with laryngeal malignancy were staged clinically according to TNM staging and they were advised to do CT scan neck contrast from skull base to mediastinum and the predictors like

i) Cartilage invasion

ii) Extra laryngeal spread

iii) Thyroid gland involvement, is compared with MRI scan and histopathology

Patients with doubtful cartilage invasion were subjected to do MRI limited cuts (3 TESLA MRI limited STIR sequence High resolution axial sections were done through the larynx) with region of interest being laryngeal cartilages, to confirm the cartilage invasion.

Short tau inversion recovery (STIR) also known as **short T1 inversion recovery** is a fat suppression technique with an inversion timeTI = T1 ln2, where the signal of fat is zero.

Confirmed cartilage invasion were planned for total laryngectomy, partial pharyngectomy, Hemi/total thyroidectomy +/- concomitant neck dissection +/- Tracheo-oesophageal puncture under general anaesthesia and the post laryngectomy specimens were marked and sent for histopathological examination.

Considering histopathological (HPE) report as gold standard, the study compares HPE with clinical predictors and imaging like CT scan neck contrast from skull base to mediastinum and MRI limited cuts.

RESULTS AND ANALYSIS

1. **Sex ratio of the study population**:

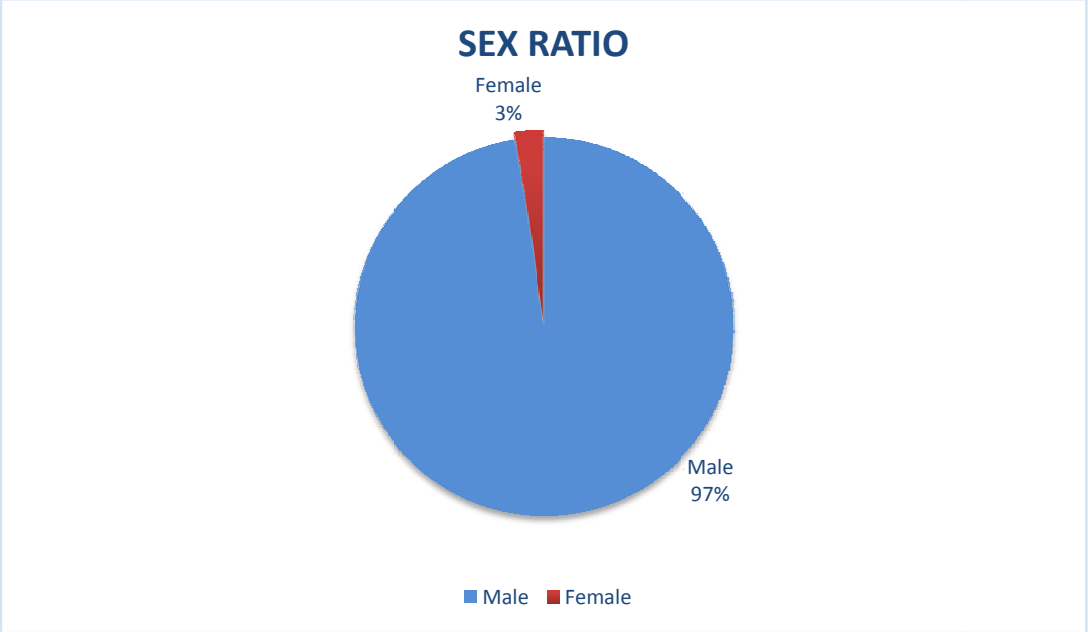


Fig. **shows sex ratio of the study population**

Of the forty study population, thirty nine (97%) cases were male and one case (3%) was female.

2. Age distribution pattern:

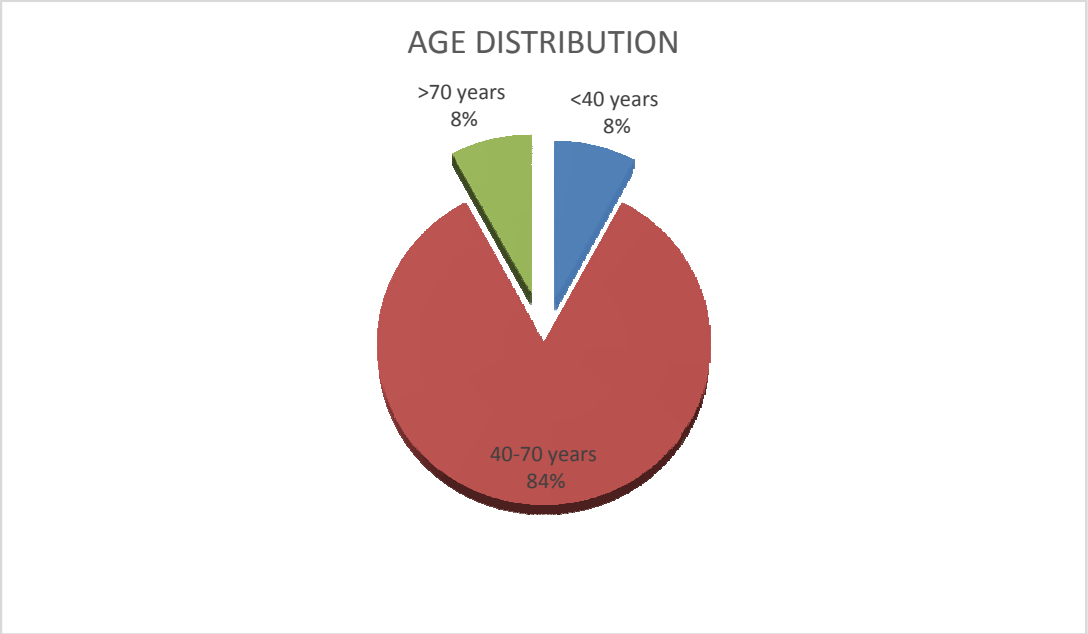


Fig. **shows Age distribution pattern of laryngeal and hypo pharyngeal cancers**

The age range was 35 years to 82 years with a mean age of 74 years. Of the total 40 patients, 8% were found to be less than 40 years of age, 84% of patients were between 40 to 70 years, and 8% were found to be more than 70 years of age.

3. Distribution of various types of laryngeal cancers:

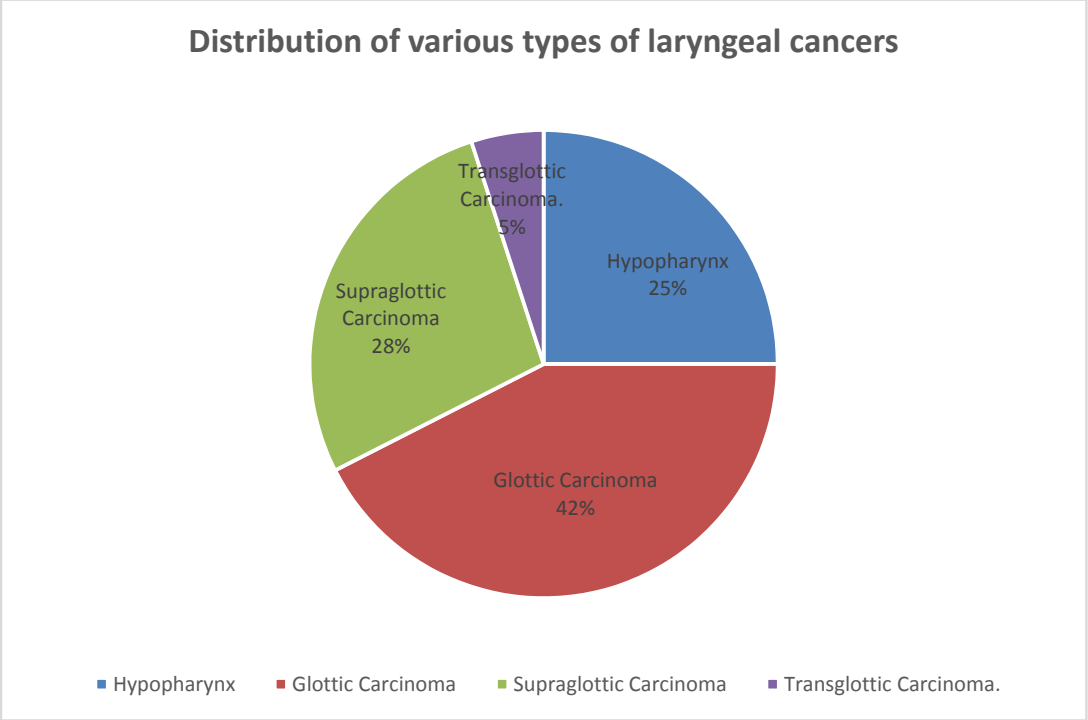


Fig. shows Distribution of various types of cancers

Of the forty cases, nineteen cases were found to be glottic carcinoma, ten cases were carcinoma Hypopharynx, eleven cases were supraglottic carcinoma and two were transglottic carcinoma.

4. Distribution of Cartilage invasion in CT scan:

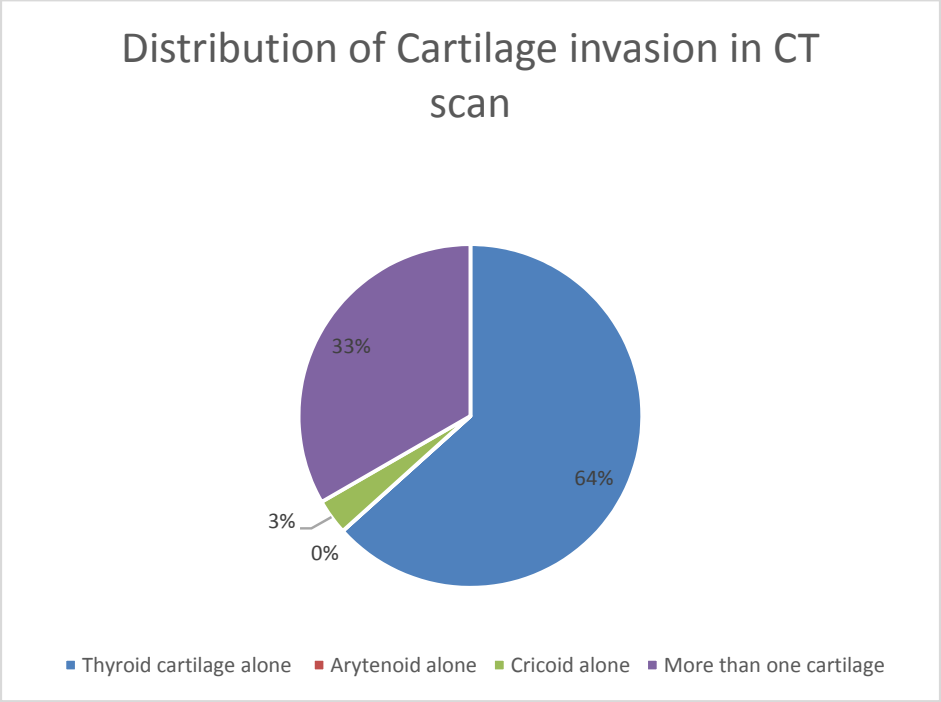


Fig. shows Distribution of laryngeal cartilage invasion in Computed Tomography scan

Of the forty cases of laryngeal cancer who were subjected to contrast enhanced computed tomography of neck from skull base to mediastinum, thyroid cartilage alone was involved in 19 cases, there were no cases with the arytenoid cartilage alone involved. One patient had the cricoid alone involved and more than one cartilage was involved in ten cases. There were eight cases with no involvement (erosion) of any laryngeal cartilages on CT scan. Six of these cases were post RT recurrences. Two cases were planned for initial radiation therapy since CT scan did not show cartilage invasion.

5. Accurate clinical predictor of cartilage invasion in CT neck Contrast Versus Histopathology

Table. Pathologically Observed Thyroid Cartilage Findings Versus CT Signs					
	Thyroid Cartilage: CT Signs				
Pathology	Normal	Sclerosis	Invasion	Penetration	Totals
Normal	2	4	0	2	8
Invasion	3	0	1	2	6
Penetration	3	5	1	17	26
Total	8	9	2	21	40
	Cricoid Cartilage: CT Signs				
	Normal	Sclerosis	Destruction	Total	
Normal	15	6	8	29	
Invasion	1	1	1	3	
Penetration	1	4	3	8	
Total	17	11	12	40	
	Arytenoid Cartilage: CT Signs				
	Normal	Sclerosis	Destruction	Total	
Normal	15	12	4	31	
Invasion	2	3	0	5	
Destruction	1	1	2	4	
Total	18	16	6	40	
Abbreviation: CT, computed tomography.					

Table. Predictive Value of Thyroid cartilage involvement CT Versus Pathologic Results			
True disease status(HPE)	Test result(CT)		
	Negative	positive	Total
Normal	6	2	8
Abnormal	11	21	32
Total	17	23	40
Predictive Values			
Parameter	% [95% confidence limits]		
Positive predictive value	91.3% [72% 98.9%]		
Negative predictive value	35.3% [14.2% 61.7%]		
False positive	2.63 [.77 8.95]		
Odds ratio	5.73 [1.09 .]		
False negative	0.458 [.246 .855]		
Sensitivity	65.6% [46.8% 81.4%]		
Specificity	75% [34.9% 96.8%]		
Abbreviation: CT, computed tomography. HPE, histopathology			

Table. Predictive Value of Cricoid cartilage involvement CT Versus Pathologic Results			
True disease status	Test result		
	Negative	positive	Total
Normal	21	8	29
Abnormal	7	4	11
Total	28	12	40
Predictive Values			
Parameter	% [95% confidence limits]		
Positive predictive value	33.3% 9.92% 65.1%		
Negative predictive value	75% 55.1% 89.3%		
False positive	1.32 .495 3.51		
Odds ratio	1.5 .367 6.27		
False negative	.879 .533 1.45		
Sensitivity	36.4% 10.9% 69.2%		
Specificity	72.4% 52.8% 87.3%		
Abbreviation: CT, computed tomography. HPE, histopathology			

Table. Predictive Value of arytenoid cartilage involvement CT Versus Pathologic Results			
True disease status	Test result		
	Negative	Positive	Total
Normal	27	4	31
Abnormal	7	2	9
Total	34	6	40
Predictive Values			
Parameter	% [95% confidence limits]		
Positive predictive value	33.3% 4.33% 77.7%		
Negative predictive value	79.4% 62.1% 91.3%		
False positive	1.72 .374 7.93		
Odds ratio	1.93 .345 11.4		
False negative	.893 .614 1.3		
Sensitivity	33.3% 4.33% 77.7%		
Specificity	79.4% 62.1% 91.3%		
Abbreviation: CT, computed tomography. HPE, histopathology			

Of the forty studied population,

a) Thyroid cartilage invasion were present in twenty three cases on CT scan, but thyroid cartilage invasion were found to be thirty two cases in histopathogy. CT scan did not pick up thyroid cartilage invasion in nine cases.
b) Cricoid cartilage invasion were present in four cases on CT scan, but cricoid cartilage invasion were found to be eleven cases on histopathogy. CT scan did not pick up cricoid cartilage invasion in seven cases.

c) Arytenoid cartilage invasion were present in two cases on CT scan, but arytenoid cartilage invasion were found to be nine cases on histopathogy. CT scan did not pick up arytenoid cartilage invasion in seven cases.

6) Accurate clinical predictor of cartilage invasion in MRI vs. Histopathology

Table. Pathologically Observed Thyroid Cartilage Findings Versus MRI additional					
	Thyroid Cartilage: Histopathology				
MRI ADDITIONAL	Normal	invasion	Penetration	total	
Normal	1	0	2	3	
Sclerosis	2	0	0	2	
Destruction	0	1	4	5	
Total	3	1	6	10	
	Cricoid Cartilage: Histopathology				
MRI	Normal	invasion	Destruction	Total	
Normal	1	0	2	3	
Invasion	3	2	0	5	
Destruction	1	0	1	2	
Total				10	
	Arytenoid Cartilage: histopathology				
MRI	Normal	Sclerosis	Destruction	Total	
Normal	1	0	2	3	
Invasion	3	2	0	5	
Destruction	1	0	1	2	
Total	5	2	3	10	
Abbreviation: CT, c1omputed tomography.					

Table. Predictive Value of Thyroid cartilage involvement limited MRI Versus HPE			
MRI	HPE		
	Normal	abnormal	Total
Normal	4	1	5
Abnormal	1	4	5
Total	5	5	10
Predictive Values			
Parameter	% [95% confidence limits]		
Positive predictive value	66.7% 22.3% 95.7%		
Negative predictive value	75% 19.4% 99.4		
False positive	2 .627 6.38		
Odds ratio	6 .441 .		
False negative	.333 .0502 2.21		
Sensitivity	80% 28.4% 99.5%		
Specificity	60% 14.7% 94.7%		
Abbreviation: MRI, Magnetic resonance imaging. HPE, histopathology			

Table. Predictive Value of cricoid cartilage involvement limited MRI Versus CT scan			
MRI SCAN	HPE		
	Normal	Abnormal	Total
Normal	1	2	3
Abnormal	2	5	7
Total	3	7	10
Predictive Values			
Parameter	% [95% confidence limits]		
Positive predictive value	33.3% .84% 90.6%		
Negative predictive value	14.3% .361% 57.9%		
False positive	.214 .0295 1.56		
Odds ratio	.0833 0 1.44		
False negative	2.57 .505 13.1		
Sensitivity	14.3% .361% 57.9%		
Specificity	33.3% .84% 90.6%		
Abbreviation: MRI, Magnetic resonance imaging. HPE, histopathology			

Table. Predictive Value of arytenoid cartilage involvement limited MRI Versus HPE			
MRI	HPE		
	Negative	positive	Total
Normal	1	2	3
Abnormal	1	6	7
Total	2	8	10
Predictive Values			
Parameter	% [95% confidence limits]		
Positive predictive value	60% 14.7% 94.7%		
Negative predictive value	20% .505% 71.6%		
False positive	.643 .199 2.07		
Odds ratio	.375 0 4.8		
False negative	1.71 .306 9.61		
Sensitivity	42.9% 9.9% 81.6%		
Specificity	33.3% .84% 90.6%		
Abbreviation: MRI, Magnetic resonance imaging. HPE, histopathology			

In ten cases in whichthere was doubtful cartilage invasion in CT scan,additional MRI was done. Thyroid cartilage invasion was present in five cases both on MRI scan and histopathology.

Seven cases had cricoid cartilage invasion on both MRI scan and histopathology.Eight case had arytenoid cartilage invasion on MRI but seven cases on histopathology. MRI had one false positive result.

7) Accurate clinical predictor of cartilage invasion in CT neck Contrast vs. MRI limited cuts

Table. Cartilage Findings MRI additional Versus CT Signs					
	Thyroid Cartilage: CT Signs				
MRI ADDITIONAL	Normal	Sclerosis	Invasion	Penetration	Totals
Normal	1	1	0	0	2
Sclerosis	2	1	0	0	3
Destruction	0	0	3	2	5
Total	3	2	3	2	10
	Cricoid Cartilage: CT Signs				
MRI	Normal	Sclerosis	Destruction	Total	
Normal	2	1	0	3	
Invasion	4	0	1	5	
Destruction	1	0	1	2	
Total	7	1	2	10	
	Arytenoid Cartilage: CT Signs				
MRI	Normal	Sclerosis	Destruction	Total	
Normal	1	1	0	2	
Invasion	2	4	1	7	
destruction	0	0	1	1	
Total	3	5	2	10	
Abbreviation: CT, computed tomography.					

Table. Predictive Value of thyroid cartilage involvement limited MRI cuts Versus CT scan			
True disease status	Test result		
	Negative	positive	Total
Normal	5	0	5
Abnormal	0	5	5
Total	5	5	10
Predictive Values			
Parameter	% [95% confidence limits]		
Positive predictive value	100% 47.8% 100%		
Negative predictive value	100% 47.8% 100%		
False positive	. . .		
Odds ratio	. 6.78 .		
False negative	0 . .		
Sensitivity	100% 47.8% 100%		
Specificity	100% 47.8% 100%		
Abbreviation: MRI, Magnetic resonance imaging. HPE, histopathology			

Table. Predictive Value of cricoid cartilage involvement limited MRI cuts Versus CT scan			
CT scan	MRI		
	Negative	positive	Total
Positive	7	1	8
Negative	1	1	2
Total	8	2	10
Predictive Values			
Parameter	% [95% confidence limits]		
Positive predictive value	100% 47.8% 100%		
Negative predictive value	100% 47.8% 100%		
False positive	. . .		
Odds ratio	7 0 .		
False negative	0 . .		
Sensitivity	100% 47.8% 100%		
Specificity	100% 47.8% 100%		
Abbreviation: MRI, Magnetic resonance imaging. HPE, histopathology			

Of the ten cases, in which MRI scan was compared with contrast enhanced CT scan of neck thyroid cartilage invasion were present in five cases on both CT and MRI scan.

Cricoid cartilage invasion were present in two cases on CT scan, while MRI showed cricoid cartilage invasion in seven cases. CT scan failed to predict cricoid cartilage invasion in five cases.

Arytenoid cartilage invasion were present in two cases on CT scan, while MRI showed arytenoid cartilage invasion in eight cases. CT scan failed to predict arytenoid cartilage invasion in six cases.

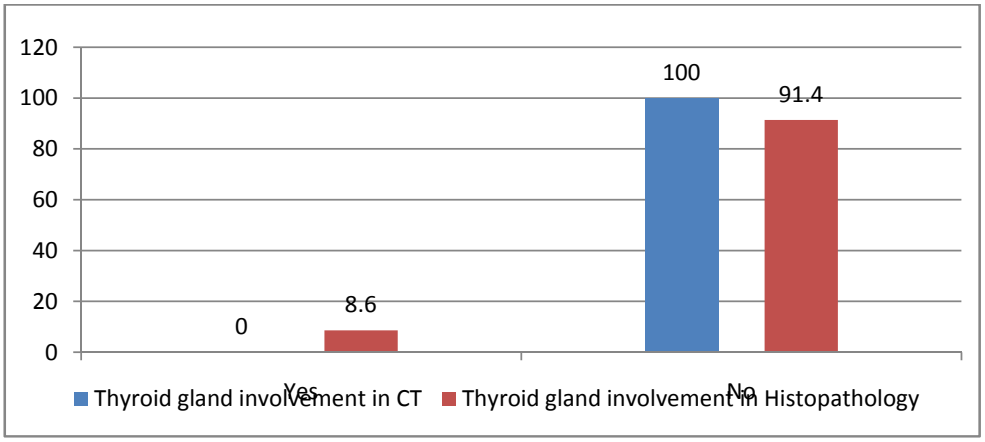
8) Accurate clinical predictor of extra laryngeal spread in CT neck Contrast vs. Histopathology

Table. Predictive Value of CT Detected Extra laryngeal Spread Versus Pathologic Results			
	CT Findings		
Pathology	Yes	No	Total
Yes	12	8	20
No	7	13	20
Total	19	21	40
Predictive Values			
Parameter		%	
Parameter		% [95% confidence limits]	
Positive predictive value		63.2 [38.4 83.7]	
Negative predictive value		60 [36.1 80.9]	
False positive		1.63 [.818 3.24]	
Odds ratio		2.57 [.722 9.16]	
False negative		.633 [.335 1.2]	
Sensitivity		60 [36.1 80.9]	
Specificity		63.2 [38.4 83.7]	
Abbreviation: CT, computed tomography. HPE, histopathology			

Of the forty cases studied, extra laryngeal spread were present in twenty cases on histopathology and extra laryngeal spread was present in nineteen cases on CT scan. So CT scan failed to predict extra laryngeal spread in one case. CT scan showed false positivity in seven cases.

9) Comparison of thyroid gland involvement in CT neck with Histopathology

Table. Predictive Value of CT Thyroid gland involvement Versus Pathologic Results			
	HPE		
CT SCAN	Yes	no	Total
Yes	0	4	4
No	2	34	36
Total	2	38	40
Parameter		% [95% confidence limits]	
Positive predictive value		0 [0 60.2]	
Negative predictive value		91.4 [76.9 98.2]	
False positive		0 [. .]	
Odds ratio		0 [0 12.9]	
False negative		1.13 [1 1.26]	
Sensitivity		0 [0 70.8]	
Specificity		88.9 [73.9 96.9]	
Abbreviation: CT, computed tomography. HPE, histopathology			



Of the forty cases, only four patients had thyroid gland involvement on CT scan and 2 of the 40 had thyroid gland involvement on Histopathology. Of the four patients where the CT scan showed infiltration of the thyroid gland, none had thyroid gland involvement on histopathology. In two patients where thyroid gland was involved on histopathology, CT scan failed to pick up the thyroid gland involvement.

Those two patients with histologically proven thyroid gland involvement were diagnosed as transglottic malignancy with cartilage erosion and extra laryngeal spread.

DISCUSSION

Cancer of the larynx is the second most common malignancy of the upper aero digestive tract. This accounts for approximately 1.7% of all new cancer diagnosis. In India, laryngeal carcinoma constitutes 2.63% of all body cancers. It is ten times more common in males than females. Smoking, alcohol, chemical exposure, laryngopharyngeal reflux and viral etiology especially HPV virus are considered as the risk factors associated with laryngeal cancer [(36)]. Tobacco and alcohol are two aetiological factors for the development of Head and Neck Squamous Cell Carcinoma (HNSCC), both independently and synergistically. The glottic region is frequently affected. The indications for laryngectomy in the management of laryngeal cancers are cartilage erosion, extra laryngeal spread and a non-functional larynx. The 1991 publication of the Veterans Administration (VA) Laryngeal Trial brought about the paradigm shift in the management of care for patients with advanced laryngeal cancer. Until then, total laryngectomy was performed as an initial treatment for most patients with T3-T4 laryngeal cancers, and thereafter non- surgical organ preservation became the standard of care. The Radiation Therapy Oncology Group 91-11 (RTOG 91-11) demonstrated that concurrent chemo-radiotherapy produced higher laryngeal preservation rates and improved local control, when compared to induction chemotherapy and hence now is consideredthe standard of care.

The purpose of our study was to assess the reliability of Computed tomography to preoperatively predict T4 disease of the larynx. In our study,40 patients who were

diagnosed with laryngeal cancers were subjected to contrast enhanced CT scan of the neck from skull base to mediastinum. The imaging was reviewed by head and neck radiologists and specific details pertaining to sclerosis, invasion, penetration and extra laryngeal spread were co-related to the findings noted on histopathology.

All statistical analyses were performed using SPSS software (SPSS Inc., Chicago, IL). Alpha error was set to 0.05 and 95% confidence intervals (CIs) were calculated. Characteristics of patients with or without thyroid gland involvement were compared using chi-square tests for categorical variables and independent sample t tests for continuous variables.

The total number of calculated sample size using chi square test is 41, however only40 cases were obtained. Thirty nine (97%) patients were male and one (3%) was female .38 of these underwent laryngectomy. Two cases underwent primary radiotherapy. One of the patient had absence of cartilage invasion on CT and MRI and another case was unresectable in view of prevertebral muscle involvement. Of the thirty eight cases, thirty two cases were primary upfront laryngectomies and the remaining six cases were salvage laryngectomies for post RT recurrences.

Considering age, our patients fell between the third decades to the eight decadewith a mean of 74 years. Of the total 40 patients, 8% were less than 40 years of age, the majority(84%)were between 40 to 70 years, and 8% were more than 70 years of age. Nineteen patients had glottic carcinoma, ten patients had carcinoma

hypopharynx, eleven patients had supraglottic carcinoma and two had transglottic carcinoma

Myung Woul Han et al studied 32 cases of laryngeal cancer, in which 2 had thyroid cartilage involvement[38]. In these patients both the CT scan and histopathology showed cartilage involvement. One of the patients had cricoid and arytenoid cartilage involvement on histopathology and radiology. In his study both computed tomography and histopathology had same sensitivity.

In a similar study of 107 cases done by Jonathan J. Beitler et al, he noted thyroid cartilage involvementin 30 cases both on CT scan and histopathology[39]. The cricoid cartilage was involved in eleven cases and arytenoid cartilage was involved in six cases on CT scan and histopathology. These studies highlighted a equal sensitivity between computed tomography and histopathology. In our study of the forty cases, computed tomography revealed thyroid cartilage involvementin twenty three cases, however significantlythirty two cases had thyroid cartilage invasion on histopathogy. Thus CT showed a false negative in 9cases. Similarly cricoid cartilage involvement was seen in only 4 cases on CT scan in contrast to 11 cases on histology.

Histopathologic analysispicked up 9 cases of arytenoid cartilage involvement whereas CT scan revealed only 2 cases of arytenoid involvement. Thus CT failed to pick up 7 cases of cricoid involvement and arytenoid cartilage involvement each.

Of the ten cases in which doubtful cartilage invasion on CT scan was suspected, magnetic resonance imaging 3Tesla STIR sequence axial cuts through the larynx were obtained. Thyroid cartilage invasion was noted in five cases both on MRI scan and histopathology.MRI picked all seven cases which had cricoid cartilage invasion as confirmed by histopathology. However MRI showed arytenoid cartilage involvement in 8 cases although histopathology confirmed only seven cases. Hence MRI had a higher false positivity in detecting arytenoid cartilage involvement.We compared the sensitivity, specificity, positive predictive value and negative predictive value of CT scan in our study with a study done by Myung Woul Han et al.

CT Scan	Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
	Myung et al	Our study	Myung et al	Our study	Myung et al	Our study	Myung et al	Our study
Thyroid cartilage	57.1	65.6	94.4	75	88.9	91.3	73.9	35.5
Cricoid cartilage	50.0	36.4	89.3	72.4	40.0	33.3	92.6	75
Arytenoid cartilage	33.3	33.3	75.9	79.4	12.5	33.3	91.7	79.4

A meta-analysis of the major studies proved that the accuracy of MR imaging is better than CT scanning on a McNemar test with a p value of 0.06. Many authors therefore recommend MR imaging as the primary modality in evaluating cartilage involvement in patients with laryngeal carcinomas.

Meta-analysis of ability of MRI to assess laryngeal cartilage				
Reference	True positive	False positive	True negative	False negative
Zbaren et al, 1997 [29]	59	25	81	3
Becker et al, 1995 [21]	55	22	118	7
Zbaren et al, 1996 [28]	52	24	69	3
Zbaren et al, 1997 [27]	44	30	94	3
Castelijns et al, 1988 [24]	33	5	38	4
Total	243	106	400	20

Sensitivity-92.4%; specificity -79.1%;

Accuracy- 83.6% (643 of 769).

In our study where we utilised a 3teslaMRI STIR sequence axial cutsto assess the larynx,MRI had a higher sensitivity in predicting thyroid cartilage erosion. In contrast to the above mentioned studies we looked at the sensitivity and specificity of MRI in each of the 3 subsites i.e thyroid cartilage, cricoid cartilage and arytenoid cartilage. MRI had 100% sensitivity in detecting thyroid cartilage invasion.

Regarding extralaryngeal spread, Myung et al, in his study of 32 patients, concluded that CT was able to detect spread in 5 cases which was confirmed by histopathology.

In our study, where 20 patients had extra laryngeal spread on histopathology, only 19 were detected with a pre-operativeon CT scan.

However in 7 cases where CT scan revealed extralaryngeal spread, the histopathology findings were contra indicatory of the same.Thus CT scan showed false positivity in seven cases.

In the 5 cases of extralaryngeal spread confirmed both by CT and histopathology by Myung et al, only one had thyroid cartilage invasion. In our study, extra laryngeal spread was present in CT scan without laryngeal cartilage invasion in 7 cases. This can be explained by the extralaryngeal spread of tumours through the thyrohyoid membrane.

Comparison of Predictive Value of CT Detected Extra laryngeal Spread		
CT Scan	%	
	Jonathan et al	Our Study
Sensitivity	49	60
Specificity	92	63.2
Positive predictive value	81	63.2
Negative predictive value	71	60

In regard to thyroid gland involvement, we compared the involvement of the gland on the basis of CT findings and histopathology. In our study conducted in our hospital between April 2014 to August 2015,which included retrospective cases from 2013, only 4 of the 40 patients had thyroid gland involvement on CECT. None of these four had thyroid gland involvement on histopathology. In two others of the 40 there was thyroid gland involvement on histopathology. In these two patients CT scan failed to pick up thyroid gland involvement. These two patients with histologically

proven thyroid gland involvement were found to have transglottic tumours with cartilage erosion and extra laryngeal spread.

In a study done by Ohad Hilly et al, thyroidectomy along with laryngectomy was performed in 52 patients. Thyroid gland involvement was evident in 21 %(11 patients) of the 88% who underwent total laryngectomy with thyroidectomy[33].
In his study, CT detected thyroid gland involvementin 1 of 11 patients, whereas the surgical specimen showed thyroid involvement in 3 of the 11 cases[40].

In another study done by L. Gaillardin et al, thyroid gland invasion were correlated with cartilage invasion. Of the eighty seven cases studied, Eleven (12.6%) of the 87 patients had histological evidence of thyroid gland invasion. Six of these 11 patients had laryngeal cancerand five patients had hypopharyngeal cancer. Five patients had thyroid gland involvement with thyroid cartilage invasion and five patients had cricoid cartilage invasion and thyroid gland involvement[41].However in our study only two patients with transglottic carcinomas had thyroid gland infiltration on histopathology.

Transglottic tumours have a higher incidence of extra laryngeal spread as pointed in a study by Sandeep P. Nayak et al[43]. He emphasised that that transglottic growths and extra laryngealsoft tissue infiltration to be statistically significantfactors that would warrant an ipsilateral hemithyroidectomyduring total laryngectomy. Numerous studies have indicated that transglottic tumours are large volume lesions that tend to spread laterally and that there is an increasedrisk of thyroid gland invasion for these tumours.

CONCLUSION

In our study, aPrimary laryngectomy was done in patients where cartilage invasion was noted on imaging and in individuals where extra laryngeal spread of tumour was evident without cartilage involvement.Salvage Laryngectomies were also done in irradiated individuals with post RT recurrences where conservative/ endoscopic or open partial laryngectomies were not possible.

Contrast enhanced Computed tomography scan helped in identification of thyroid cartilage invasion accurately in 91.3 % of cases and this has immensely contributed in the staging and treatment planning of Stage 3 and Stage 4 laryngeal cancers. The addition of a 3tesla MRI scan STIR sequence axial cuts through the larynx in our studyimproved the accuracy and aided in detecting cartilage erosion in these cases. We therefore conclude that 3 Tesla MRI limited high resolution axial section should be considered as routine protocol for all patients in whom there is doubtful cartilage invasion on contrast enhanced CT scan. Since only limited cuts are done both the costs involved and time factors are kept to a minimum. All patients in our study in whom laryngectomy was done had one of the laryngeal cartilage invaded on CT scan or MRI scan or had extra laryngeal spread except post RT recurrences.

Our study showed that 3 tesla MRI STIR sequence axial cuts scan should also be consideredto evaluate all patients where cartilage erosion is clinically suspected but not confirmed on CT scan and also in patients where CT scan shows extra

laryngeal spread without any obvious cartilage invasion. The sensitivity of detecting extra laryngeal spread in CT scan was only 60%.

In our study we looked at the indications for ipsilateral thyroidectomy in patients undergoing total laryngectomy. Contrast enhanced CT scan suggested thyroid gland infiltration in four out of the forty cases. Histopathology was negative in all these four cases.Two other cases showedthyroid gland infiltration on histopathology but not on CT scan. These two cases were with thyroid gland involvement on histopathology were both transglottic tumours with extra laryngeal spread. Hence an ipsilateral hemithyroidectomy is probably still indicated in transglottic cancer with cartilage invasion and/or extra laryngeal spread.

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APPENDIX

1. Consent forms

2. Patient information sheet

3. Proforma

4. Data Analysis sheet

5. Colour plates

CONSENT FORMS AND INFORMATION SHEET

Christian Medical College, Vellore

Department of Oto-rhino-laryngology

Clinical predictors of cartilage invasion in laryngeal cancer,extra laryngeal spread and thyroid gland involvement in patients undergoing total laryngectomy.

You are being requested to participate in a study. In this study we will be examining you clinically a complete ENT and head & neck examination including an indirect laryngoscopy and flexible laryngoscopy. If you are diagnosed to have cancer you will be subjected to a CT scan and posted for direct laryngoscopy and biopsy to confirm the diagnosis. If your biopsy confirms cancer, you will be given the option of surgery to remove the tumour. This surgery is called total laryngectomy and will be done with/without concomitant operation to also remove the lymph nodes and thyroid gland.

What is indirect laryngoscopy and flexible laryngoscopy?

Indirect laryngoscopy is routine part of investigation,if patient come with complaints of hoarseness and difficulty in swallowing.We use a mirror to look at your voice box

as an indirect image. We spray 10% xylocaine in your throat to anaesthetize throat to make the test comfortable. In this test we are asked to put your tongue out and we hold the tongue and see your larynx. If indirect laryngoscopy test has any findings,we asked to do flexible laryngoscopy scopy to confirm the diagnosis.Flexible laryngoscopy is done by passing a very tiny camera through your nose in to the throat to examine your voice box and swallowing passage.

If you take part what will you have to do?

As mentioned above you have to go through the complete ENT and head & neck examination, indirect laryngoscopy, flexible laryngoscopy and CT scan.These tests are done as a routine protocol of management for all patients suspected to have cancer of the voice box. All other treatments that you are already on will be continued and your regular treatment will not be changed during this study. No additional procedures or blood tests will be conducted routinely for this study. There is no extra cost which you have to pay for this study.If at any time you experience any problems, you will be expected to report this to the doctor.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you since these are commonly done test. We are unable to provide any monetary compensation, however.

Will you have to pay for the test?

You have to pay for all the tests, since this is a routine protocol of management. Any other treatment that you usually take will continue.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask

Dr.M.Mohamed Abdul Kathar

04162282075

drkadharshaji@gmail.com

CONSENT TO TAKE PART IN A CLINICAL TRIAL

Study Title: To evaluate the accurate clinical predictors of cartilage invasion and extra laryngeal spread and thyroid gland involvement in patients with laryngeal and hypo pharyngeal cancers (stage 3 and stage 4)

Study Number:

Participant's name:

Date of Birth / Age (in years):

I_____

_____, son/daughter of _____

(Please tick boxes)

Declare that I have read the information sheet provide to me regarding this study and have clarified any doubts that I had. [ ]

I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]

I also understand that the test will be provided at free of cost

I understand that I will receive free treatment for any study related injury or adverse event but I will not receive and other financial compensation [ ]

I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]

I understand that my identity will not be revealed in any information released to third parties or published [ ]

I voluntarily agree to take part in this study [ ]

Name:

Signature:

Date:

Name of witness:

Relation to participant:

Date:

PROFORMA

NAME OF THE PATIENT:

AGE:

SEX:

DIAGNOSIS:

BIOPSY REPORT :

SURGERY: DONE/NOT DONE

HEAD & NECK EXAMINATION: YES/ NO

a) LARYNGEAL FRAME WORK SPLAYING

b) LARYNGEAL CREPITUS

c) NECK NODE

d) THYROID GLAND PALPABLE

INDIRECT LARYNGOSCOPY: YES/ NO

-ANTERIOR COMMISSURE INVOLVEMENT

-LATERAL HYPOPHARYNGEAL WALL INVOLVEMENT

NASOPHARYNGOLARYNGOSCOPY: YES/ NO

-ANTERIOR COMMISSURE INVOLVEMENT

-LATERAL HYPOPHARYNGEAL WALL INVOLVEMENT

CT NECK CONTRAST FROM SKULL BASE TO MEDIASTINUM YES/ NO

1. Cartilage invasion

a) Thyroid

b) Arytenoids

c) Cricoid

2. Extra laryngeal spread

-Strap muscles

-Thyroid gland involvement

MRI LIMITED CUTS DONE/NOT DONE

CARTILAGE INVASION

a) Thyroid cartilage

b) Cricoid cartilage

c) Arytenoid cartilage

HISTOPATHOLOGY YES/NO

1. Cartilage invasion

a) Thyroid cartilage

b) Arytenoid cartilage

c) Cricoid cartilage

2. Extra laryngeal spread

-Strap muscles

-Thyroid gland involvement

DATA ANALYSIS SHEET

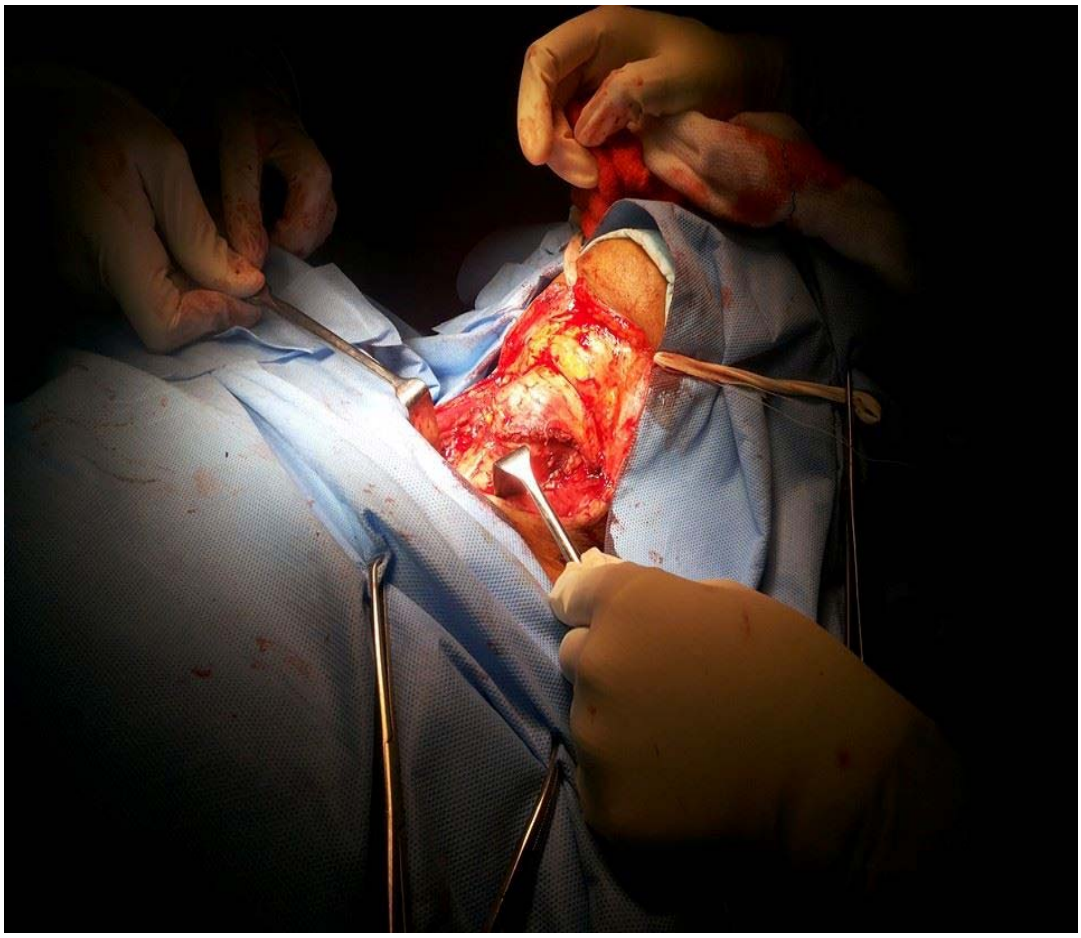
NAME	AGE	SEX	HOSP NO	THYROID CARTILAGE										
				HISTOPATHOLOGY				CT SCAN			MRI ADDITIONAL CUTS			
				NORMAL	INVASION	PENETRATION	NORMAL	SCLEROSIS	INVASION	PENETRATION	NORMAL	SCLEROSIS	DESTRUCTION	NORMAL
			065453G	2	2	1	1	2	2	2				1
			043361G	2	1	2	1	2	2	2				1
			097118G	2	2	1	2	2	1	2				1
			346977F	2	2	1	1	2	2	2				2
			055128G	2	1	2	2	2	1	2				1
			937054F	2	1	2	1	2	2	2				1
			050599G	2	2	1	2	2	2	1				1
			147159G	1	2	2	2	1	2	2				2
			119902G	2	2	1	2	1	2	2				1
			939096F	2	2	1	2	2	2	1				1
			233599G	2	2	1	2	2	2	1	2	2	1	1
			759528F	2	2	1	2	2	2	1				1
			087768G	1	2	2	1	2	2	2				1
			689439D	2	2	1	2	1	2	2				2
			628929F	1	2	2	2	2	2	1				1
			242256G	2	2	1	2	2	2	1				1
			251858G	1	2	2	2	1	2	2	2	1	2	2
			842542D	1	2	2	2	1	2	2	1	2	2	2
			151219G		SURGERY NOT DONE		2	1	2	2	1	2	2	SURGERY N
			176198G	2	2	1	2	2	2	1	2	2	1	1
			959593F		SURGERY NOT DONE		1	2	2	2	1	2	2	S
			215976G	2	2	1	2	2	2	1	2	2	1	1
			222140G	2	2	1	2	2	2	1				1
			199227F	2	2	1	2	2	2	1				1
			759985F	2	2	1	2	2	2	1	2	2	1	2
			815673F	2	2	1	2	1	2	2				1
			858811F	2	2	1	2	2	2	1				1
			871437F	1	2	2	1	2	2	2	2	1	2	1
			905728D	2	2	1	2	2	2	1				1
			774905F	2	2	1	2	2	2	1				1
			787478F	2	1	2	1	2	2	2				1
			764469F	1	2	2	2	2	2	1				1
			726819F	2	2	1	2	2	2	1				1
			340507F	1	2	2	2	1	2	2				1
			628192F	2	1	2	2	2	2	1				1
			480959A	2	2	1	2	1	2	2				1
			645247F	2	2	1	2	2	2	1				2
			905728D	2	2	1	2	2	2	1				1
			212255G	2	2	1	2	2	2	1				1
			236984G	2	1	2	2	2	2	1	2	2	2	1

idnoidenti	namenamı	ageagepati	sexsexapti	hspnohosp	hspnohosp	dxdiagnosi	bxbiopsyre	hnescsplay	hnelclaryn	hnennneck	hnethythyı	idlacanter	idllhwlate	nplacanter	npllhwlate	ctnacanter	ctnlhwlate	ctncicarti	ctnsmstrap	ctnthythyr	ctnnnodali	mrcicarti	hpeacantei	hpelhwlate	hpecicarti	hpesmstra	hpethythyı	hpennnodal
1	AVIJIT DUT	56	1	65453	G	CA LEFT PF	MPD. TO P	1	2	2	2	2	1	2	1	2	1	1	1	1	2		2	2	1	2	2	1
2	KARTHIK CI	62	1	43361	G	CA GLOTTI	MOD DIFF	2	1	2	2	2	2	2	2	1	2	1	2	2	2		2	2	2	2	2	2
3	SURYA BAI	68	1	97118	G	CA TRANSC	MOD. TO P	2	1	1	2	2	2	2	2	1	2	1	2	2	1		1	1	1	1	2	1
4	TARUN KUI	51	1	346977	F	CA RIGHT (	MOD.DIFF	2	1	2	2	2	2	2	2	1	2	1	2	2	2		1	2	1	2	2	2
5	RAMAKRIS	61	1	55128	G	CA HYPOPI	POORLY DI	2	2	1	2	2	2	2	2	2	1	2	2	2	1		1	2	1	2	2	1
6	MANI	56	1	937054	F	CA GLOTTI	MOD DIFF	2	2	2	2	2	2	2	2	1	2	1	1	2	2		1	2	1	2	2	2
7	BANAMALI	55	1	50599	G	CA GLOTTI	MOD.DIFF	2	2	2	2	2	2	2	2	1	2	1	1	2	2		1	2	1	1	2	2
8	BRAMMAI	53	1	147159	G	CA HYPOPI	SARCOMA	2	2	2	2	2	2	2	1	2	1	1	2	1	2		2	2	2	2	2	2
9	KRISHNA K	55	1	119902	G	CA SUPRAC	POORLY DI	1	1	2	2	2	2	2	2	2	2	1	2	2	2		1	2	1	2	2	2
10	SHAJAHAN	56	1	939096	F	CA GLOTTI	MOD .DIFF	2	1	2	2	2	2	2	2	2	2	1	1	1	2		1	2	1	2	2	2
11	SWAPAN K	46	1	233599	G	CA GLOTTI	MOD.DIFF.	1	1	1	2	2	2	2	2	2	2	2	1	2	1	1	2	2	1	1	2	2
12	MAKRIUS K	48	1	759528	F	CA SUPRAC	WELL TO M	2	1	1	2	2	2	2	2	1	2	1	2	2	1		1	2	1	1	2	1
13	DEVASHISI	45	1	87768	G	CA SUPRAC	MOD.DIFF.	2	1	2	2	2	2	2	2	1	2	2	2	2	2		1	2	1	2	2	1
14	KALYAN KU	57	1	689439	D	CARCINOM	MOD.DIFF.	2	2	2	2	2	2	2	2	1	2	1	2	2	2		1	2	1	1	2	2
15	RANJIT THA	39	1	628929	F	CA SUPRAC	MOD.DIFF	1	2	2	2	2	2	2	2	2	2	2	1	2	1		1	2	1	1	2	1
16	SUBBANNA	69	1	242256	G	CA HYPOPI	MOD.DIFF	1	2	1	2	2	1	2	1	2	1	2	1	2	1		2	1	1	1	2	2
17	KALPANA (	50	2	281858	G	CA GLOTTI	MOD.DIFF	2	1	2	2	2	2	2	2	2	2	2	2	2	2	1						
18	BANESWAI	72	1	842542	D	CA SUPRAC	POORLY DI	2	1	1	2	2	2	2	2	2	1	1	2	2	1	2	2	1	2	2	2	2
19	DAK BAHAI	47	1	151219	G	CA RIGHT F	POORLY DI	2	1	1	2	2	2	2	1	2	2	2	1	2	1	2						
20	MOHAMM	60	1	176198	G	CA SUPRAC	MOD DIFF	2	1	1	2	2	2	2	2	1	2	2	1	2	1	1	1	2	1	1	2	2
21	MUNUSAM	65	1	959593	F	CA GLOTTI	WELL DIF S	2	1	2	2	2	2	2	2	1	2	1	1	2	2	1						
22	BIPIN BIHA	56	1	215976	G	CA SUPRAC	POORLY DI	1	1	2	2	2	2	2	2	2	2	2	1	2	1	1	2	2	1	1	2	1
23	MOHAMM	49	1	222140	G	TRANSGLO	WELL DIFF	2	2	2	2	2	2	2	2	2	2	1	1	2	2		1	2	1	2	1	2
24	MIR MOHA	37	1	199227	F	CA GLOTTI	MOD DIFF	2	1	2	2	2	2	2	2	1	2	1	1	2	2		1	2	1	1	2	2
25	MANOHAR	62	1	759985	F	CA SUPRAC	MOD.DIFF.	2	1	2	2	2	2	2	2	1	2	2	2	2	2	1	1	2	1	2	1	2
26	JOTINDRAI	70	1	815673	F	CA RIGHT F	MOD.TO PI	2	2	2	2	2	1	2	1	2	1	1	1	2	2		2	1	1	1	2	2
27	SHYAMAL (	59	1	858811	F	CA SUPRAC	MOD.DIFF.	2	1	2	2	2	2	2	2	2	1	1	1	2	2		2	1	1	1	2	2
28	MURUGES/	67	1	871437	F	CA GLOTTI	MOD.DIFF	2	1	2	2	1	2	1	2	1	2	2	2	2	2	1	1	2	1	2	2	2
29	NAGESHW.	63	1	905728	D	CARCINOM	MOD.DIFF	1	2	2	2	2	2	2	2	1	2	1	2	2	2		1	2	1	1	2	1
30	MOHAMM	38	1	774905	F	CA GLOTTI	MOD.DIFF	2	1	2	2	2	2	1	2	1	2	1	2	2	2		1	2	2	2	2	2
31	LALAMPUL	45	1	787478	F	CA RIGHT F	POORLY DI	2	2	2	2	2	2	2	1	2	1	1	2	2	2		2	1	1	2	2	2
32	MURUGAS.	64	1	764469	F	CA RIGHT I	MOD.DIFFI	2	2	1	2	2	2	2	2	2	1	2	2	2	1		2	2	2	2	2	2
33	RAM SHAR	73	1	726819	F	CA GLOTTI	MOD.DIFF	1	1	2	2	2	2	2	2	1	2	1	1	2	1		1	2	1	1	2	1
34	NAGESHW.	48	1	340507	F	CA RIGHT \	HIGH GRAI	2	1	2	2	2	1	2	2	1	2	2	2	2	1		1	2	1	1	1	1
35	NABARD JC	35	1	628192	F	CA RIGHT S	MOD.DIFF.	2	1	2	2	2	2	2	2	2	2	1	1	2	2		2	2	2	2	2	2
36	JESUDASAI	68	1	147819	F	CARCINOM	POORLY DI	1	1	1	2	2	2	2	2	1	2	1	1	2	2		1	2	1	1	2	2
37	GOUR HAR	68	1	480959	A	CA SUPRAC	POORLY DI	1	1	2	2	2	2	2	2	2	2	2	1	2	2		1	2	1	1	2	2
38	SUNDAR PI	74	1	645247	F	CA OF HYP	MOD.DIFF.	2	1	2	2	2	2	2	2	2	2	1	2	1	1		2	2	1	1	2	1
39	NAGESHW.	63	1	905728	D	CA GLOTTI	MOD.DIFF.	1	1	2	2	2	2	2	2	1	2	1	2	2	1		1	2	1	1	2	1
40	CHANDAN	65	1	212255	G	CARCINOM	MOD.DIFF	1	1	2	2	2	2	1	2	1	2	1	1	2	2		1	2	1	2	2	2
41	BIMAL KAN	53	1	236984	G	CARCINOM	MOD.DIFF	2	2	2	2	2	2	2	2	1	2	1	1	2	2	1	1	1	1	2	2	2

COLOUR PLATES

COLOUR PLATE 1

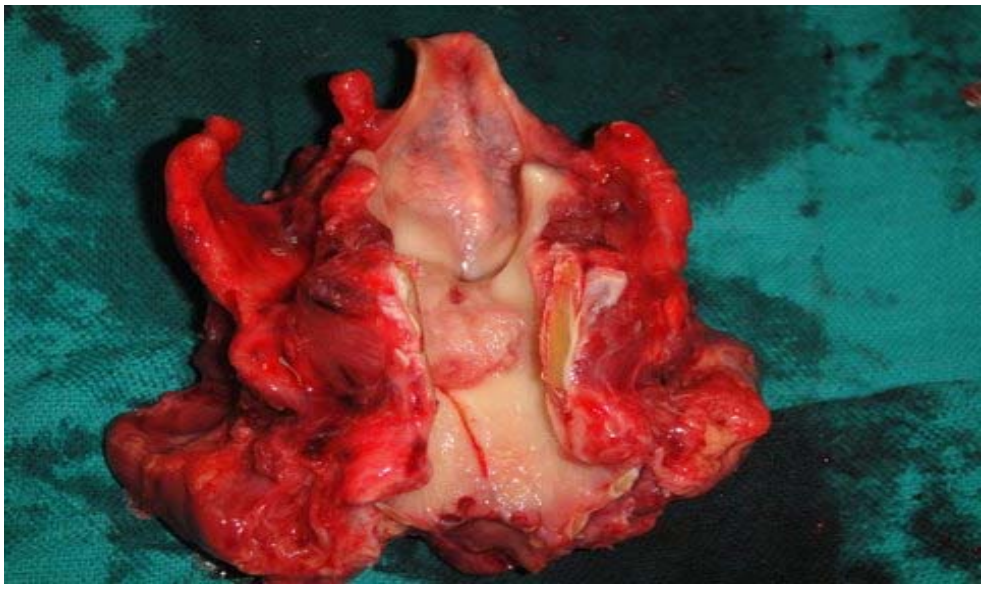
Patient undergoing total laryngectomy with partial pharyngectomy and hemithyroidectomy and primary Tracheo-oesophageal puncture by our head and neck team



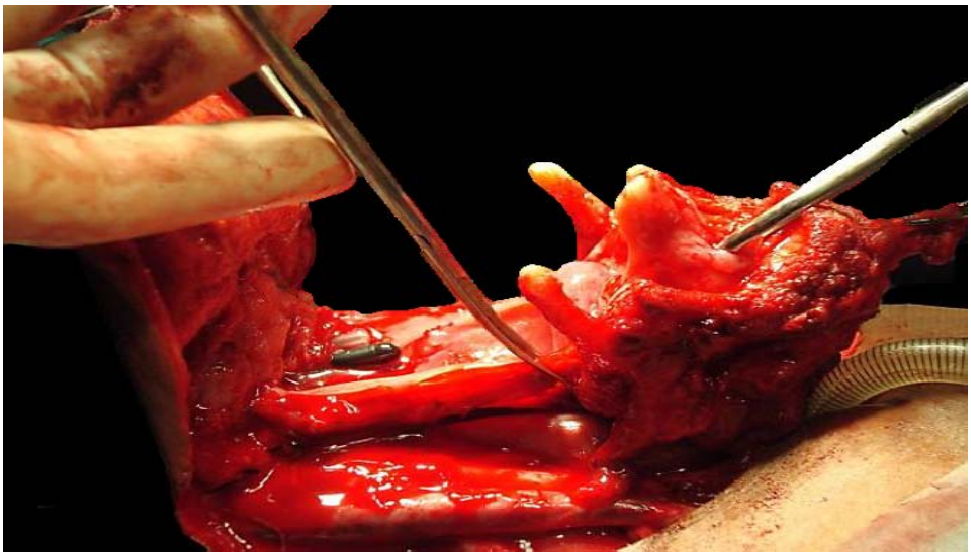
COLOUR PLATE 2

Histopathological analysis:

Whole organ serial sections were studied in axial plane and final histopathological staging arrived which is compared with radiological and clinical staging (AJCC, TNM)



COLOUR PLATE 3: Total laryngectomy specimen



Colour plate 4: Laryngectomy specimen for histopathology sent in every case after assessing tumour extension macroscopically